# In the United States Court of Federal Claims

**OFFICE OF SPECIAL MASTERS**

Filed: October 27, 2023

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| DESTANIE HARGROVE, as Mother on behalf of A.F.M., | * | |
| Petitioner, | * | No. 17-233V |
| v. | * | Special Master Dorsey |
| SECRETARY OF HEALTH AND HUMAN SERVICES, | * | Entitlement; Diphtheria-Tetanus-Acellular-Pertussis ("DTaP") Vaccine; Epilepsy; Seizures; Encephalopathy. |
| Respondent. | * | |

Rick Alan Cory, Danks & Danks, Evansville, IN, for Petitioner.
Colleen Clemons Hartley, U.S. Department of Justice, Washington, DC, for Respondent.

## DECISION[1]

## I. INTRODUCTION

On February 17, 2017, Destanie Hargrove, as Mother, on behalf of A.F.M., ("Petitioner") filed a petition under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2018).[2] Petitioner alleges A.F.M. suffered "table[]

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), Petitioners have 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2018) ("Vaccine Act" or "the Act"). All citations in this Decision to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

injuries, including, but not limited to, severe static epileptic encephalopathy and permanent brain damage resulting from adverse effects of one or more . . . vaccinations received on May 7, 2014," including diphtheria-tetanus-acellular-pertussis ("DTaP"), hepatitis B ("Hep B"), inactivated polio vaccine ("IPV"), Haemophilus influenzae type b ("Hib"), and Rotavirus. Petition at 1 (ECF No. 1).[3] Respondent argued against compensation, stating that "this case is not appropriate for compensation under the terms of the Act." Respondent's Report ("Resp. Rept.") at 2 (ECF No. 38).

**A**fter carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards,[4] the undersigned finds that Petitioner has failed to provide preponderant evidence that A.F.M.'s DTaP vaccine caused her condition. Thus, Petitioner has failed to satisfy her burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, the petition must be dismissed.

## II. ISSUES IN DISPUTE

First, the parties dispute whether the initial event experienced by A.F.M. on May 8, 2014 was a seizure or an apparent life-threatening event ("ALTE"). See Joint Prehearing Statement of Facts and Issues ("Joint Prehearing Submissions"), filed Apr. 10, 2022 (ECF No. 99).

The next issue is whether A.F.M. suffered a Table injury. Petitioner's Motion for Ruling on the Record ("Pet. Mot."), filed Apr. 23, 2021, at 1, 12 (ECF No. 80). As acknowledged by Respondent, the alleged Table injury is based on the question of whether A.F.M. suffered an "encephalopathy." Resp. Response to Pet. Mot. ("Resp. Response"), filed Aug. 13, 2021, at 21 (ECF No. 83) (citing 42 C.F.R § 100.3(a)(II)(B)). In the alternative, Petitioner asserts a causation-in-fact claim in which Petitioner may be entitled to compensation if she shows by preponderant evidence that A.F.M.'s injury was caused-in-fact by the DTaP vaccination she received on May 7, 2014. Pet. Mot. at 1. The parties disagree about whether Petitioner has provided preponderant evidence of causation for all three Althen prongs. See Joint Prehearing

[3] Petitioner subsequently narrowed her allegation to assert Table and causation-in-fact claims for injuries caused by the DTaP vaccination on May 7, 2014, and not the other vaccinations A.F.M. received that day. See Petitioner's Motion for Ruling on the Record ("Pet. Mot."), filed Apr. 23, 2021, at 1, 12 (ECF No. 80). Therefore, the undersigned references only the DTaP vaccination going forward except when describing the opinions of Dr. Holmes when he uses the term "vaccinations."

[4] Although this Decision discusses some but not all of the medical literature in detail, the undersigned reviewed and considered all of the medical records and all of the medical literature submitted in this matter. See Moriarty v. Sec'y of Health & Hum. Servs., 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); Simanski v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), aff'd, 601 F. App'x 982 (Fed. Cir. 2015).

Submissions at 1; Pet. Mot. at 6, 25; Resp. Response at 21-26; Althen, 418 F.3d at 1280.

## III. BACKGROUND

### A. Procedural History

Petitioner filed her petition on February 17, 2017, and filed medical records in the following months.[5] Petition; Pet. Exhibits ("Exs.") 1-36. Respondent filed his Rule 4(c) Report arguing against compensation on December 11, 2017. Resp. Rept. at 2.

On March 15, 2018, Petitioner filed an expert report from Dr. Marcel Kinsbourne. Pet. Ex. 37. Respondent filed an expert report from Dr. Gregory Holmes on June 7, 2018. Resp. Ex. A. In October 2018 and February 2019, the parties filed supplemental expert reports from Dr. Kinsbourne and Dr. Holmes, respectively. Pet. Ex. 39; Resp. Ex. C. At a status conference held on May 1, 2019, the special master assigned to the case presented additional questions for the experts to opine on. Order dated May 6, 2019 (ECF No. 51). From June 2019 to January 2021, the parties filed responsive expert reports from Dr. Kinsbourne and Dr. Holmes. Pet. Exs. 40-44; Resp. Exs. D-G.

Throughout this time, the parties entertained settlement discussions but ultimately requested a ruling on the record. See ECF Nos. 57, 72, 71. On April 23, 2021, Petitioner filed her motion for a ruling on the record. Pet. Mot. Respondent filed a response on August 13, 2021, and Petitioner filed a reply on September 13, 2021. Resp. Response; Pet. Reply to Resp. Response ("Pet. Reply"), filed Sept. 13, 2021 (ECF No. 84).

Upon reassignment of the case to the undersigned, a status conference was held on February 10, 2022. See Notice of Reassignment dated Feb. 7, 2022 (ECF No. 87); Order dated Feb. 10, 2022 (ECF No. 88). The undersigned acknowledged the case was ripe for a ruling on the record; however, after review of the evidence, she opined that given the complexity of the issues with this case, a hearing would be very helpful. Order dated Feb. 10, 2022, at 2. The parties agreed to a remote hearing. Id. Prior to the hearing, Respondent confirmed that he wished to defend the case and was not interested in settlement discussions. Resp. Status Rept., filed Apr. 18, 2022 (ECF No. 106).

An entitlement hearing was held via videoconference on May 17, 2022. See Order dated May 18, 2022 (ECF No. 112); Transcript ("Tr.") 1. Dr. Kinsbourne and Dr. Holmes testified at the hearing. Tr. 3. On October 31, 2022, Petitioner filed a post-hearing brief. Pet. Post-Hearing Brief ("Pet. Br."), filed Oct. 31, 2022 (ECF No. 122). Respondent filed a post-hearing brief on March 3, 2023, and Petitioner filed a reply on March 23, 2023. Resp. Post-Hearing Submission ("Resp. Br."), filed Mar. 3, 2023 (ECF No. 125); Pet. Reply to Br. in Further Support of Compensability of Pet. Claim ("Pet. Reply Br."), filed Mar. 23, 2023 (ECF No. 126).

This matter is now ripe for adjudication.

[5] Petitioner continued to file medical records throughout the course of litigation.

## B. Factual History

### 1. Summary of Medical Records[6]

A.F.M., a female, was born full-term on October 24, 2013, by a vaginal delivery. Pet. Ex. 8 at 18.[7] She weighed seven pounds, three ounces at birth. Id. Her newborn screening was normal. Pet. Ex. 7 at 1.[8] A.F.M. received a Hep B vaccination on the date of her birth. Pet. Ex. 8 at 17.

Following A.F.M.'s birth, Petitioner presented A.F.M. for regular pediatric well-child visits at eight-days old, one-month old, and two-months old with her pediatrician, Dr. Larry Crick. See Pet. Ex. 7 at 2-12. The assessments on these dates were normal. Id. On January 27, 2014, A.F.M. received the Pediatrix (DTaP, Hep B, IPV), Hib, and Rotavirus vaccinations. Id. at 13.

On May 7, 2014, A.F.M. returned to Dr. Crick's office for her six-month physical examination. Pet. Ex. 7 at 15-19. A.F.M. was examined that day by Sharon Shields, advanced practice registered nurse ("APRN"). Id. A.F.M. presented with a cough and runny nose, but was developmentally appropriate and her examination was normal. Id. In connection with the visit, A.F.M. received the subject vaccinations—Pediatrix (DTaP, Hep B, IPV), Hib, and Rotavirus. Id. at 17.

The next day, on May 8, 2014, A.F.M. was taken by ambulance to Methodist Hospital emergency department ("ED"), as she was reportedly "limp and staring off at ceiling" and was "not responsive initially." Pet. Ex. 8 at 47-110. The emergency medical responders ("EMS") indicated that A.F.M. was not responding appropriately upon their arrival, but she became more alert during transport. Id. It was noted that A.F.M. received routine vaccinations the day before. Id.

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[6] The medical record summary is taken directly from Respondent's Rule 4(c) Report, which the undersigned finds fairly and accurately depicts the events described in the medical records. Resp. Rept. at 2-14. For an additional detailed summary of the medical records, see Dr. Holmes' initial expert report. Resp. Ex. A at 1-19.

[7] Exhibit 8 (ECF No. 6-9) as outlined in Petitioner's exhibit list is the "Birth records and Post-Injury records from Methodist Hospital." These records were Bates-stamped as "Exhibit 4." Hereinafter, the undersigned, like Respondent, will refer to the birth records and post-injury records from Methodist Hospital as "Exhibit 8." ECF No. 6-9.

[8] Exhibit 7 (ECF No. 6-8) as outlined in Petitioner's exhibit list is the "Vaccine, Pre-Injury and Post-Injury records from Dr. Larry Crick." These records were Bates-stamped as "Exhibit 5." Hereinafter, the undersigned, like Respondent, will refer to Dr. Crick's records as "Exhibit 7." ECF No. 6-8.

At the ED, A.F.M. was alert and in no distress. Pet. Ex. 8 at 47-110. A.F.M.'s physical examination was normal. Id. A.F.M. was admitted overnight for observation for upper respiratory infection ("URI"), an episode of altered mental status ("suspect possibly secondary to a reflux or chocking episode, but she did not have any cyanosis"),[9] and possible urinary tract infection ("UTI"). Id. at 67-68.

During her overnight observation,[10] A.F.M.'s lab results displayed an abnormal liver function test with a mildly elevated serum glutamic-oxaloacetic transaminase ("SGOT") and an alkaline phosphatase of 247 (normal 50-136). Pet. Ex. 8 at 56-57. A.F.M. had an elevated white count on complete blood count ("CBC") of 15.19 (normal 4.8-10.8), elevated platelet count of 542,000 (normal up to 400,000), and an increase in the percentage of bands to 24 (normal 0-11). Id. A.F.M.'s urinalysis was abnormal with positive nitrite and leukoesterase and 2+ bacteria. Id. A.F.M.'s chest X-ray was negative. Id. at 88. A.F.M.'s urine culture was positive for *Escherichia coli* ("*E. coli*"). Id. at 86. On May 9, 2014, A.F.M.'s discharge diagnoses included a UTI and URI. Id. at 47. A.F.M.'s physical examination was normal at the time and the hospitalist recommended that A.F.M. have an outpatient electroencephalogram ("EEG") to rule out a seizure. Id. at 83.

On May 13, 2014, A.F.M. presented for an EEG which displayed normal results. Pet. Ex. 8 at 111. On May 15, 2014, A.F.M. returned to her pediatrician, Dr. Crick, for follow-up from her hospital discharge and EEG. Pet. Ex. 7 at 23-27. Dr. Crick noted that A.F.M. had experienced no problems since her hospital discharge and that she continued to take antibiotics because her urine culture grew *E. coli*. Id. A.F.M.'s physical examination was normal, and she was assessed with a UTI. Id.

On May 22, 2014, A.F.M. experienced another episode of "altered mental status" and presented to Dr. Crick. Pet. Ex. 7 at 28-31. Petitioner reported that A.F.M. "stared upward with [her] mouth open and her face was red" and then her behavior normalized within five minutes. Id. Dr. Crick assessed A.F.M. with gastroesophageal reflux ("GERD"), he noted that her cystitis (UTI) was resolved, and he wanted to "[rule out] [s]eizures." Id. Dr. Crick prescribed Ranitidine for GERD. Id. at 5.

On June 16, 2014, A.F.M. returned to Dr. Crick's office for a seven-month, well-child visit. Pet. Ex. 7 at 32-36. A.F.M. was "pulling at her left ear" on arrival. Id. On examination, A.F.M. achieved all expected developmental milestones. Id. A.F.M. was taking Ranitidine, ibuprofen, and hydroxyzine (as needed for nasal congestion). Id. Nurse Shields noted that "A.F.M.'s parents are very concerned the Pertussis component of her combination immunization

[9] Cyanosis is "a bluish discoloration, especially of the skin and mucous membranes due to excessive concentration of deoxyhemoglobin in the blood." Cyanosis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=12098 (last visited Oct. 16, 2023).

[10] During the observation period, A.F.M.'s grandmother inquired as the "contents of vaccination from a couple days before." Pet. Ex. 8 at 83.

may have caused a perceived seizure in May of 2014." Id. Further, Nurse Shields noted that "[w]hile the EEG was negative and there was a greater concern for a choking episode related to Reflux[,] the pertussis vaccine will be eliminated for the time being and dosing for vaccines will be administered on an alternative schedule." Id. A.F.M. received Rotavirus and diphtheria tetanus ("DT") vaccinations at this visit. Id.

Six days later, on June 22, 2014, A.F.M. presented to the ED at Union County Methodist Hospital for a seizure. Pet. Ex. 10 at 1-15.[11] En route to the ED, A.F.M. became unresponsive. Id. at 6. On arrival to the ED, A.F.M. was responding to touch and slightly crying. Id. Petitioner reported that A.F.M. had a history of seizures for three months. Id. Petitioner further reported that A.F.M. "received the TDAP [three] months ago and had a seizure about [one] week later" and that A.F.M. "had TD immunization on Monday and seizure today." Id. at 5. A.F.M.'s initial white count on CBC was elevated at 17.49 (4-10 nl), and she was transferred to St. Mary's Medical Center ("SMMC") pediatric intensive care unit ("ICU") for a higher level of care. Id.

From June 22 to June 25, 2014, A.F.M. was hospitalized at SMMC for new onset seizures and a UTI.[12] Pet. Ex. 9 at 1-5.[13] On arrival at SMMC, A.F.M. was "completely at her baseline." Id. at 3. She was "alert, happy, responsive[,] and completely nontoxic on exam." Id. A.F.M. did not have a fever. Id. The hospital physician, Dr. Taveepong Terayanont pursued a seizure work-up, as it was reported that this was the third episode. Id. at 7. A head computerized tomography ("CT") and chest X-ray were normal. Id. at 3. A.F.M.'s brain magnetic resonance imaging ("MRI") was also normal. Id. While A.F.M.'s EEG during the hospitalization did not display frank epileptiform discharges, it was noted that "in the correct clinical context may be associated with a predisposition towards partial seizures or partial seizures with secondary generalization, but this must be carefully correlated clinically." Id. at 3.

Following the EEG, a physician at SMMC consulted with a neurologist at Kosair Children's Hospital ("Kosair"). Pet. Ex. 9 at 3. The Kosair neurologist recommended that A.F.M. start Keppra. Id. A.F.M.'s urine culture was positive for *E. coli*, and she was started on amoxicillin. Pet. Ex. 9 at 36. A renal ultrasound was ordered, which displayed a probable right extrarenal pelvis and thickening of the urinary bladder wall, probable cystitis. Id. at 40-42. At discharge, Petitioner was instructed to have A.F.M. follow-up with Kosair pediatric neurology

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[11] Exhibit 10 (ECF No. 6-11) as outlined in Petitioner's exhibit list is the "Post-Injury records from Union County Methodist Hospital." These records were Bates-stamped as "Exhibit 7." Hereinafter, the undersigned, like Respondent, will refer to the post-injury records from Union County Methodist Hospital as "Exhibit 10." ECF No. 6-11.

[12] It was noted during this hospitalization that A.F.M.'s grandmother believed that "A.F.M. [was] having seizures after vaccines and is possibly allergic to something in the shot." Pet. Ex. 9 at 63.

[13] Exhibit 9 (ECF No. 6-10) as outlined in Petitioner's exhibit list is the "Post-Injury records from St. Mary's Medical Center." These records were Bates-stamped as "Exhibit 6." Hereinafter, the undersigned, like Respondent, will refer to the post-injury records from St. Mary's Medical Center as "Exhibit 9." ECF No. 6-10.

and her pediatrician. Id. at 5.

On June 29, 2014, A.F.M. experienced a seizure episode and presented to Methodist Hospital Union County ED. Pet. Ex. 10 at 16-19. A.F.M. was transferred to Kosair for further work-up. Pet. Ex. 11 at 1-253.[14]

On admission to Kosair, A.F.M.'s Keppra dosage was increased, she was treated for her UTI, and a video EEG was completed. See Pet. Ex. 11 at 1-253. The video EEG documented a 25-minute focal seizure, during which time A.F.M. was interactive. Id. at 3-9. A.F.M. also had a four-minute generalized tonic-clonic seizure associated with desaturation, requiring Ativan and a bag-valve-mask ventilation for recovery. Id. The neurology service noted that A.F.M.'s "family [was] very concerned these 'seizures' [were] a result of her DTaP vaccine that she received one day prior to initial onset of symptoms." Id. at 30. The neurology service diagnosed A.F.M. with focal epilepsy, recommended a further increase of Keppra, and ordered Diastat as needed. Id. at 35. A.F.M. was discharged on July 2, 2014. Id.

Later the same day, A.F.M. presented to Methodist Hospital ED due to two reported seizures since her discharge from Kosair. Pet. Ex. 8 at 115-42. A.F.M. was tearful and irritable, and she was transported by ambulance to the pediatric ICU at SMMC. Id.

On admission to SMMC, it was noted that A.F.M. had a history of a seizure disorder that had been "detected roughly [two] weeks ago." Pet. Ex. 9 at 76-77. A.F.M. displayed daily seizures at SMMC that initially responded to increased Keppra. Id. Then, A.F.M. required endotracheal intubation for airway protection and the hospitalist believed that her condition required transfer to a tertiary care center with an inpatient pediatric neurology team. Id. On July 5, 2014, A.F.M. was transferred to Vanderbilt Children's Hospital ("Vanderbilt") for further treatment. Id.

From July 5 to September 12, 2014, A.F.M. was hospitalized at Vanderbilt and underwent an extensive work-up. Pet. Ex. 12 at 16-22.[15] Upon arrival to Vanderbilt, A.F.M. was alert, but ten minutes later, she suffered a seizure lasting 140 minutes. Id. at 1045-49. Thereafter, A.F.M. was placed in a pentobarbital coma. Id. A.F.M.'s genetics work-up for epilepsy was unrevealing. Id. at 16. On August 27, 2014, a gastric tube ("G-tube") was placed following reduced oxygen saturations with feeding and aspiration. Id. A.F.M.'s brain MRI displayed "restricted diffusion involving bilateral hippocampi with mild surrounding edema."

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[14] Exhibit 11 as outlined in Petitioner's exhibit list is the "Post-Injury records from Kosair Children's Hospital." These records were Bates-stamped as "Exhibit 8." Hereinafter, the undersigned, like Respondent, will refer to the birth records and post-injury records from Kosair Children's Hospital as "Exhibit 11."

[15] Exhibit 12 as outlined in Petitioner's exhibit list is the "Post-Injury records from Vanderbilt Monroe Carell Jr. Children's Hospital." These records were Bates-stamped as "Exhibit 9." Hereinafter, the undersigned, like Respondent, will refer to the post-injury records from Vanderbilt Monroe Carell Jr. Children's Hospital as "Exhibit 12."

Id. From September 4 to September 6, 2014, A.F.M. underwent a two-day EEG, which displayed "seizures involving right parieto-temporo-occipital region." Id. at 1075. At the time of discharge on September 12, 2014, A.F.M.'s primary diagnosis was epilepsy and secondary diagnosis was hypoxemia. Id. at 16.

Following discharge, A.F.M. was admitted to Cardinal Hill Rehabilitation from September 12 to September 18, 2014. Pet. Ex. 13 at 2-7.[16] On admission, A.F.M.'s history was noted as "beginning around June 2014 patient started having seizures that became increasingly frequent." Id. During rehabilitation, A.F.M. had two to three seizures a day without desaturations below 80%, and all resolved in less than four minutes without medications. Id. Thereafter, Petitioner and her mother requested that A.F.M. be transferred to University of Kentucky Children's Hospital ("UK") for continuous EEG monitoring. Id. A.F.M. was stable at the time of discharge. Id.

Accordingly, on September 18, 2014, A.F.M. was transferred to UK and remained inpatient until September 25, 2014. Pet. Ex. 11 at 683-715. Without the results of the genetic testing from Vanderbilt, neurologist Dr. Kimberley Jones noted that the most likely explanation for A.F.M.'s seizures and neurocognitive decline was an "underlying genetic disorder, either a channelopathy or mitochondrial disorder." Id. at 715. Likewise, Dr. Donita Lightner noted concern about a metabolic or genetic disease during the hospitalization. Id. at 704-05. On September 25, 2014, the discharge diagnoses included "intractable multifocal epilepsy" with "[s]uspected West syndrome[,] infantile spasms [and] hypsarrhythmia on EEG," "[e]ncephalopathy," and "[b]ehavioral regression . . . [l]ikely secondary to intractable epileptic seizures compounded by [medications]." Id. at 695.[17]

On October 1, 2014, A.F.M. presented to SMMC by ambulance, having reportedly suffered 22 seizures that day. Pet. Ex. 9 at 408. The ED physician noted that A.F.M.'s neurologic baseline was declining and she recently had a G-tube placed for feeds. Id. at 404. A.F.M. was then transferred to Kosair by air ambulance for further evaluation. Id.

A.F.M. remained inpatient at Kosair from October 2 to October 9, 2014. Pet. Ex. 11 at 256-60. Following an extensive examination, pediatric neurologist Dr. Vinay Puri's impression was that A.F.M. was suffering from infantile spasms and cryptogenic epilepsy with malignant migrating seizures of infancy. Id. at 275-77. Dr. Puri noted that A.F.M. likely had an "underlying epilepsy of unidentified etiology that progressed and now likely has post-seizure encephalopathy due to prolonged seizures (140 minute seizure on 7/5/2014)." Id. at 275. Dr.

[16] Exhibit 13 as outlined in Petitioner's exhibit list is the "Post-Injury records from Cardinal Hill Rehabilitation." These records were Bates-stamped as "Exhibit 10." Hereinafter, the undersigned, like Respondent, will refer to the post-injury records from Cardinal Hill Rehabilitation as "Exhibit 13."

[17] Again, A.F.M.'s grandmother noted concerns that vaccines caused her seizures and she also questioned molds and parasites. Pet. Ex. 11 at 683. The family noted that they were upset with the treatment at Vanderbilt and think they are responsible for her current neurologic status. Id.

Puri also noted that A.F.M.'s genetic work-up had been unrevealing as to a genetic cause for her epilepsy. Id. Moreover, Dr. Puri reviewed the genetic test (EpiSEEK) gene analysis from Vanderbilt, which displayed two genetic variants[18] of uncertain clinical significance, as neither was associated with severe epilepsy or matched her clinical picture. Id. at 275, 659-61. On October 9, 2014, A.F.M.'s discharge diagnosis was infantile spasms and partial complex seizure disorder. Id. at 256.

Following her hospitalization, on October 13, 2014, A.F.M. had a repeat EEG, which displayed tracing consistent with hypsarrhythmia.[19] Pet. Ex. 11 at 916-17. The same day, A.F.M.'s mitochondrial whole genome sequencing testing results were reported. Pet. Ex. 32 at 5-6. A.F.M.'s testing revealed that "no large deletions or known deleterious mutations were detected." Id. The diagnosis of a mitochondrial DNA disorder could not be confirmed. Id.

Two days later, on October 15, 2014, A.F.M. presented to Methodist Hospital by emergency transport for respiratory distress. Pet. Ex. 8 at 143-67. A.F.M.'s chest X-ray displayed evidence of right lower lobe pneumonia, and she was transferred to SMMC. Id. at 164; Pet. Ex. 9 at 415-19. On admission, Dr. Puri, from Kosair, was consulted as it was noted that they were having problems controlling her airway due to severe encephalopathy and chronic intractable seizure disorder. Pet. Ex. 9 at 415-19. At that time, Dr. Puri and the SMMC hospitalist believed that palliative care would be in the best interest of the child, but the family wanted everything done, including "very aggressive care." Id. at 419. Thereafter, A.F.M. was transferred to Kosair for further treatment and the potential placement of a trach. Pet. Ex. 11 at 1027-33.

A.F.M. remained inpatient at Kosair from October 16 to October 31, 2014. Pet. Ex. 11 at 928-32. A trach was not placed. Id. A.F.M.'s discharge diagnoses included aspiration pneumonia, infantile spasms, and cryptogenic epilepsy. Id.

Following discharge from Kosair, A.F.M. returned to her pediatrician, Dr. Crick, on November 3, 2014. Pet. Ex. 7 at 37-41. Petitioner reported that A.F.M. continued to experience seizures and that A.F.M. had fluid on her liver. Id. On examination, A.F.M. had poor eye contact, non-purposeful movements, and weakness in all extremities. Id. Dr. Crick's assessment was global developmental delay, infantile spasms with intractable epilepsy, and hypotonic cerebral palsy. Id. Dr. Crick recommended a hearing examination and ophthalmology consultation with Dr. Craig Douglas. Id.

In November 2014, A.F.M. began physical therapy through First Steps. Pet. Ex. 14 at 1-

[18] The two genetic variants reviewed were RAF1 and SCN4A. Pet. Ex. 11 at 659-60.

[19] Hypsarrhythmia refers to "an electroencephalographic abnormality sometimes observed in infants, with random, high-voltage slow waves and spikes that arise from multiple foci and spread to all cortical areas. It is seen most commonly in cases of jackknife seizures." Hypsarrhythmia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=24469 (last visited Oct. 16, 2023).

2.[20] On December 24, 2014, A.F.M. returned to the Methodist Hospital ED for seizures. Pet. Ex. 16 at 9-21.

On January 21, 2015, A.F.M. had a repeat EEG, on which "no normal activity was seen," and the results were interpreted as "likely consistent with a transitional state between hypsarrhythmia and the slow spike and wave of Lennox-Gastaut syndrome."[21] Pet. Ex. 18 at 4-5.

On February 5, 2015, A.F.M. underwent an asthma evaluation with pediatric pulmonologist, Dr. Ronald Morton. Pet. Ex. 27 at 5-7. Dr. Morton's assessment was chronic lung disease, chronic pulmonary aspiration, and restrictive lung disease. Id.

A.F.M. returned to Dr. Puri on August 10, 2015 for a follow-up pediatric neurology evaluation. Pet. Ex. 31 at 27-33. At that time, Dr. Puri indicated that A.F.M.'s conditions were of an "unclear etiology." Id. An EEG study on the same date was consistent with epileptic encephalopathy, but no longer displayed findings suggestive of hypsarrhythmia. Id. at 34-35.

From September 1 to September 9, 2015, A.F.M. was hospitalized at Kosair for aspiration pneumonia, and she was treated with antibiotics. Pet. Ex. 18 at 75-84.

At 22 months of age, on September 17, 2015, A.F.M. underwent a developmental evaluation. Pet. Ex. 14 at 5-7. A.F.M.'s fine and gross motor skills were in the two-month range, her communication skills were in the three-month range, her cognitive skills were in the two-to-three-month range, and her social skills were in the three-month range. Id.

Due to feeding intolerance, A.F.M. returned to Kosair for a Nissen fundoplication with a G-tube exchange from December 14 to December 16, 2015. Pet. Ex. 18 at 472-73. While in the hospital, she was seen by pediatric urology for her neurogenic bladder with associated urinary retention. Id. at 510-15.

On July 18, 2016, A.F.M. had an initial asthma and allergy evaluation with Dr. Kelly Brauer. Pet. Ex. 23 at 4-7. Petitioner reported in A.F.M.'s "past immunization history" that she had "reaction to shots – very bad seizures." Id. Food allergy testing was completed that day and Petitioner was instructed to return with A.F.M. when the test results were available. Id.

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[20] Exhibit 14 as outlined in Petitioner's exhibit list is the "Post-Injury records from First Steps." These records were Bates-stamped as "Exhibit 12." Hereinafter, the undersigned, like Respondent, will refer to the post-injury records from First Steps as "Exhibit 14."

[21] Lennox-Gastaut syndrome is "an atypical form of absence epilepsy characterized by diffuse slow spike waves, often with atonic, tonic, or clonic seizures and intellectual disability; there may also be other neurologic abnormalities or multiple seizure types." Lennox Syndrome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=110889 (last visited Oct. 16, 2023).

On July 25, 2016, A.F.M. was admitted to Kosair for seizures with secondary diagnoses of viral illness (unspecified), metabolic acidosis, and hypernatremia. Pet. Ex. 18 at 865-69. A repeat EEG completed the same day was suggestive of a moderate diffuse encephalopathy and "may be seen in children with global developmental delays." Id. at 900. It was also suggestive of an ongoing potential towards a multifocal epilepsy disorder. Id. There was no hypsarrhythmia noted. Id. A.F.M. was discharged the next day. Id.

On August 24, 2016, A.F.M. was evaluated by pediatric ophthalmologist, Dr. Craig Douglas. Pet. Ex. 30 at 2-5. Dr. Douglas diagnosed her with cortical visual impairment and recommended follow-up in two years. Id. Dr. Douglas noted that while her vision may improve somewhat, her prognosis was extremely guarded. Id.

On September 2, 2016, A.F.M. returned to Dr. Brauer for results of her food allergy testing. Pet. Ex. 23 at 8-10. Petitioner inquired about "potential immune problems." Id. A.F.M.'s immunoglobulin ("Ig") E testing was negative for common foods. Id. Moreover, she had reassuring immunoglobulins for her age, but no appreciable pneumococcal or diphtheria titers. Id.

A.F.M. returned for a pediatric neurology evaluation with Dr. Puri on September 12, 2016. Pet. Ex. 31 at 12-18. In connection with the follow-up, Dr. Puri noted his impression that A.F.M. "had a genetic abnormality that predisposed her to having seizures after having immunizations, and that she definitely developed epilepsy encephalopathy." Id.

A.F.M. again returned to Dr. Puri on December 13, 2016, and Dr. Puri noted that "[t]he etiology of her epilepsy is likely genetic. She would benefit from more expansive genetic testing."[22] Pet. Ex. 31 at 11.

On December 19, 2016, Petitioner presented with A.F.M. to Pediatric Health Group to establish new pediatric care. See Pet. Ex. 29 at 2-8. Petitioner reported that she "believe[d] vaccine[s] cause[d] [A.F.M.'s] medical problems." Id. at 2. A.F.M. was wheelchair bound at that time. Id.

In April 2017, A.F.M. was hospitalized at St. Vincent Hospital for chronic constipation. Pet. Ex. 35 at 1-3. In addition, A.F.M. had a repeat EEG on April 27, 2017, which showed slowing of the background consistent with generalized encephalopathy and the presence of epileptiform discharges. Id. at 21-22.

### 2. Summary of Additional Records[23]

[22] It is not clear whether this recommended testing was done as no results were filed.

[23] This section includes a brief summary of specific records relevant to the factual issue or to the undersigned's Decision.

A.F.M.'s medical records establish that on May 7, 2014, the day of her DTaP vaccination, she was examined by a nurse practitioner, and noted to have a cough and runny nose, but otherwise was normal and developmentally appropriate. Pet. Ex. 7 at 15-19. The following morning, May 8, 2014, a call was placed for an ambulance at 5:34 a.m. Pet. Ex. 38 at 2. The ambulance arrived on the scene at 5:46 a.m. Id. Upon arrival, EMS found A.F.M. in her "grandmother's lap, unresponsive" with "respirations irregular and labored." Id. Lung sounds were clear, pulse was regular, and her skin was pale. Id. Pupils were dilated and non-reactive. Id. EMS did not document that A.F.M. was having seizure activity when they arrived. EMS records show that at 5:48 a.m., A.F.M. had a pulse of 140, respiratory rate of 20, and oxygen saturation of 88% on room air.[24] Id. at 1. Oxygen was administered and A.F.M.'s oxygen saturation improved to 92%. Id. At 5:54 a.m., A.F.M. was noted to be "improved." Id. Assessment documented at 5:48 a.m. revealed no mental abnormalities, no abnormalities of the head, face, eyes, or airway, and no abnormalities of lung sounds. Id. EMS departed the home at 5:59 a.m. and arrived at the ED at 6:22 a.m. Id. Again, A.F.M.'s condition was noted to be improved. Id. In their narrative notes for the event, EMS documented that A.F.M.'s "condition gradually improved to normal response for age" and remained stable for the "duration of the trip." Id.

The ED records on May 8, 2014, at 6:30 a.m. document that A.F.M.'s condition on arrival was stable, and she was alert and playful. Pet. Ex. 8 at 51, 53, 68. Her eyes were open; she was babbling and obeying commands. Id. at 52. The emergency physician (Dr. Eric Ervin) was at the bedside at 6:40 a.m. to examine A.F.M. Id. at 55. At 6:50 a.m., A.F.M. was again noted to be "awake, happy, [and] playing." Id. at 49. Neurological examination revealed that she was oriented and had no motor or sensory deficit. Id. At 10:48 a.m., A.F.M.'s condition was "good stable." Id. at 59. Dr. Ervin's impression was "[URI], episode of altered mental status, suspect possibly secondary to a reflux or choking episode, but she did not have any cyanosis. Possible [UTI]." Id. at 69.

Nursing neurological system assessment performed on May 8, 2014, at 11:35 a.m. documented that A.F.M. was alert, that her behavior was appropriate, and that her assessment was within defined neurological parameters. Pet. Ex. 8 at 90. A.F.M. was noted to be awake, cooperative, and smiling at 12:14 p.m. Id. at 93. Progress notes at 1:13 p.m., note that A.F.M. was "awake and alert, baby appear[ed] appropriate for age. Pleasant affect. No acute distress." Id. at 81. During nursing rounds at 6:29 p.m., A.F.M. was again noted to be awake and cooperative, and smiling. Id. at 94. Throughout the evening and overnight, A.F.M.'s assessments remained stable with no indication of abnormal neurological behavior. See id. at 93-100. On May 9, 2014, at 5:16 a.m., A.F.M. was "awake" and "cooperative." Id. at 89.

A.F.M. was discharged on May 9, 2014, at 9:46 a.m., and her physical examination prior to discharge was normal. Pet. Ex. 8 at 65, 71, 83. There is no indication that A.F.M. had any decreased or abnormal level of consciousness during her hospitalization. See id. On May 13, 2014, A.F.M. had an EEG, which was normal. Id. at 111. There is no indication that she had a decreased or abnormal level of consciousness at that time. See id. A.F.M. was seen by her

[24] Normal oxygen saturation is ≥ 95%; ≤ 75% is critical. Kathleen D. Pagana & Timothy J. Pagana, Mosby's Manual of Diagnostic and Laboratory Tests, 1061-62 (6th ed. 2018).

pediatrician, Dr. Crick, on May 15, 2014. Pet. Ex. 7 at 23-27. Dr. Crick documented that A.F.M. had no problems following her hospital discharge; her physical examination was normal. Id.

No recent medical records have been filed.

### C. Expert Reports

#### 1. Petitioner's Expert, Dr. Marcel Kinsbourne[25]

##### a. Background and Qualifications

Dr. Kinsbourne earned his B.A. from Christ Church at Oxford University in 1952, his Bachelor of Medicine (B.M.) and Bachelor of Surgery (B.Ch.) from Oxford University Medical School in 1955, his M.A. and Doctor of Medicine (D.M.) from Oxford University in 1956 and 1963, and his M.D. from State of North Carolina in 1967. Pet. Ex. 40 at 1. From 1955 to the early 1990s, he regularly treated patients. Id. at 1-2; Tr. 7. Throughout his career, Dr. Kinsbourne has also held teaching positions at various institutions. Pet. Ex. 40 at 2-3. Dr. Kinsbourne has held medical licenses in the United Kingdom, Canada, North Carolina, Massachusetts, and Virginia. Id. at 2. He has been bestowed numerous honors and awards, has served and is currently serving on a number of editorial boards, and has authored or co-authored more than 400 publications. Id. at 3-39.

Dr. Kinsbourne has not practiced pediatric neurology in over forty years. Tr. 30.

##### b. Opinions

Dr. Kinsbourne offered opinions related to the factual issue, whether A.F.M. experienced a seizure or an ALTE the day after vaccination. He also opined as to causation.

###### i. Initial Event May 8, 2014—Seizure vs. ALTE

At the hearing, Dr. Kinsbourne summarized the events of May 8, 2014, the day after vaccination, and concluded A.F.M. had a seizure. Tr. 10-15. A.F.M.'s medical records show that at approximately 6:30 a.m., Petitioner "saw her daughter unresponsive with [her] eyes turned up . . . and mouth open, limp, and [] struggling for breath." Tr. 10. A.F.M. was taken by ambulance to Methodist Hospital, and the "ambulance record reflected that they thought [] she [] was having a seizure." Tr. 11. Dr. Kinsbourne stated that when A.F.M. arrived at the hospital, "she had spontaneously recovered without treatment." Id. Dr. Kinsbourne testified that the physicians were "unclear as to what had happened," and they questioned whether she had choked, regurgitated, or had a seizure. Id. An EEG was ordered, and it was normal. Id. He acknowledged that A.F.M. was afebrile before the event. See Pet. Ex. 39 at 6; Tr. 53.

[25] Dr. Kinsbourne submitted six expert reports and testified at the entitlement hearing on May 17, 2022. Pet. Exs. 37, 39, 41-44; Tr. 3.

Dr. Kinsbourne agreed that when A.F.M. was discharged from the hospital, after her admission on May 8, 2014, her discharge diagnosis did not include seizure. Tr. 44. He opined that at the time, the physicians did not know what had happened, whether A.F.M.'s episode was caused by choking, apnea,[26] or infection. Id.

According to Dr. Kinsbourne, A.F.M. had a seizure on May 8, 2014, presenting as "behavioral arrest," since "the child [] stopped doing anything whatever – stopped moving, stopped making any noise – and [was] fixed in one position." Tr. 15. Dr. Kinsbourne described A.F.M. as being in a "static limbo," while having "very brief focal attacks lasting [] a minute or two or three at a time, coming in . . . [a] cluster, one after the other . . . without the child retaining full awareness or full behavior in between." Tr. 15-16. Dr. Kinsbourne also opined there was "continuous status epilepticus, which is a seizure lasting more than 30 minutes." Tr. 16.

Dr. Kinsbourne disagreed with Respondent's expert Dr. Holmes' opinion that A.F.M.'s initial event on May 8, 2014 was an ALTE. Tr. 17. According to Dr. Kinsbourne, ALTE is "not a diagnosis," but a condition that can have many different causes, including seizures. Id.; see also Pet. Ex. 42 at 1-2. He cited several articles that describe ALTE, including one by Aminiahidashti,[27] who defined it as "as an episode that is frightening to the observer . . . characterized by some combination of apnea, color change, marked change in muscle tone, choking, gagging, or coughing." Pet. Ex. 42 at 1 (quoting Pet. Ex. 42A at 1).[28] Dr. Kinsbourne disagreed that A.F.M. had "gagging, choking, coughing[,] or an obstructed airway." Id. at 2.

**1. Type and Duration of Event on May 8, 2014**

At the hearing, Dr. Kinsbourne testified that A.F.M.'s initial seizure on May 8, 2014, was a focal or "hypomotor seizure." Tr. 13-14. Prior to the hearing, however, his opinions were different and changed over the course of his six reports.

In his first expert report, Dr. Kinsbourne opined that A.F.M.'s initial seizure was an "absence seizure." Pet. Ex. 37 at 3. He defined absence seizures as "seizures that [] last just a few seconds, and are characterized by a blank or 'absent' stare." Id. (internal citation omitted). They "involve brief, sudden lapses of consciousness. . . . [and] are more common in children

[26] Apnea is the "cessation of breathing." Apnea, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=3758 (last visited Oct. 16, 2023).

[27] Hamed Aminiahidashti, Infantile Apparent Life-Threatening Events, an Educational Review, 3 Emergency 8 (2015). This is also cited as Resp. Ex. F, Tab 18.

[28] Aminiahidashti stated that ALTE is not a diagnosis, and it may be associated with various conditions, including GERD, "respiratory infections, and seizures." Pet. Ex. 42A at 2. For "reported final diagnoses for patients with apparent life-threatening events," see Pet. Ex. 42A at 2 tbl.1.

than adults." Id. (internal citation omitted). Riviello[29] explained that the "peak age of childhood absence epilepsy is from 6 to 7 [years]." Pet. Ex. 37L at 4. "The seizures consist of an abrupt cessation of ongoing activity, with a change of facial expression and a blank gaze. The duration is short, rarely lasting longer than 30 [seconds], there is no preceding aura or subsequent postictal depression, and there may be frequent automatisms." Id.

In his second expert report, Dr. Kinsbourne opined that A.F.M.'s first seizure was "nonconvulsive status epilepticus (NCSE),"[30] or in the alternative, "a complex partial status epilepticus."[31] Pet. Ex. 39 at 1. In support of this opinion, Dr. Kinsbourne cited an abstract (not the full article) by Chang and Shinnar.[32] See Pet. Ex. 39B. They defined status epilepticus as a "medical emergency" requiring "prompt recognition and treatment." Id. at 1. And they described nonconvulsive status epilepticus as a "heterogeneous disorder with varied causes and several subtypes" but there is "no universally accepted definition." Id. The two most common subtypes are absence status epilepticus and complex partial status epilepticus. Id. "The degree of mental status alteration can vary from mild confusion all the way to coma." Id. Chang and Shinnar further stated that NCSE "should be suspected in patients who fail to wake up after a convulsive seizure and in those with coma of undetermined cause." Id.

In his third and fifth expert reports, Dr. Kinsbourne again opined that A.F.M.'s first seizure was a NCSE, and stated it was a "prolonged absence seizure [that] exceeded 30 minutes in duration." Pet. Ex. 41 at 1; see also Pet. Ex. 43 at 1. Dr. Kinsbourne also clarified the definition of NCSE: "Strictly speaking, [NCSE] is only used when the seizure activity is corroborated by concurrent [EEG]." Pet. Ex. 41 at 1. A.F.M. did not have an EEG done during her episode on May 8, 2014. Pet. Ex. 43 at 2.

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[29] James Riviello, Pediatric EEG Abnormalities, in The Clinical Neurophysiology Primer 178 (A.S. Blum & S.B. Rutkove eds., 2007).

[30] NCSE is a "status epilepticus that does not include generalized tonic-clonic seizures." Nonconvulsive Status Epilepticus, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=108328 (last visited Oct. 10, 2023).

[31] Dr. Holmes opined that "complex partial status epilepticus" is a "term that is no longer used." Resp. Ex. F at 2.

[32] Andrew K. Chang & Shlomo Shinnar, Nonconvulsive Status Epilepticus, 29 Emergency Med. Clinics N. Am. 65 (2011).

In his fifth report, Dr. Kinsbourne opined that A.F.M.'s initial seizure was "atypical" for an absence seizure. Pet. Ex. 43 at 1.[33] He stated that "[e]ach individual [absence] seizure lasts no more than a few seconds" and typically "occur in clusters." Id. He further opined that because A.F.M. was limp during the initial event, it was "atypical for absence seizures." Id. He then opined that A.F.M.'s initial seizure was an "absence status" seizure, which according to Dr. Kinsbourne, is "the most common type of [NCSE]." Id. at 2 (citing Pet. Ex. 43E).[34]

Grin and DiMario stated that absence status epilepticus is "characterized by a prolonged confusional state of variable duration and severity produced by a diagnostic [EEG] spike and wave pattern." Pet. Ex. 43E at 1. Dr. Kinsbourne also cited Andermann and Robb,[35] stating that "absence status is a clearly recognizable seizure pattern but by no means a uniform one. The essential feature is a prolonged confusional state of varying severity." Pet. Ex. 43 at 2 (quoting Pet. Ex. 43A at 2). While the diagnosis is "possible on the basis of a detailed history," even without EEG, Andermann and Robb explained that the diagnosis "must be supported by the presence of generalized interictal spike and wave discharges." Pet. Ex. 43A at 2. They also found that absence status epilepticus before age 10 was rare. Id. at 5. The duration of these seizures varies; Andermann and Robb reported "episodes may last from half an hour to [two] days." Id.

Lastly, in his sixth expert report, Dr. Kinsbourne, responding to statements made by Dr. Holmes, denied that he ever opined that A.F.M. had an "absence seizure disorder." Pet. Ex. 44 at 3. Instead, he said he was describing A.F.M.'s "prolonged onset seizure," to involve "behavioral

[33] Dr. Kinsbourne cited an article by Nolan et al., regarding atypical absence seizures. Pet. Ex. 43G (Melinda Nolan et al., Clinical and Neurophysiologic Spectrum Associated with Atypical Absence Seizures in Children with Intractable Epilepsy, 20 J. Child Neurology 404 (2005)). It stated that atypical absence seizures "present with a gradual clinical behavioral change in onset and offset." Id. at 2. During the seizures "children can retain some ability for purposeful movement and speech." Id. There may be "limpness, arrest of activity, but with retention or only 'fogging' of consciousness." Id.

[34] Jennifer M. Grin & Francis J. DiMario , Absence Status Epilepticus Causing a Prolonged Acute Confusional State, 37 Clinical Pediatrics 37 (1998).

[35] F. Andermann & J.P. Robb, Absence Status: Reappraisal Following Review of Thirty-Eight Patients, 13 Epilepsia 177 (1972).

arrest without motor concomitants, which is one of the three ways in which [migrating focal seizures in infancy ("MFSI")][36] begins." Id.

Regarding the duration of the initial seizure, in his first report, Dr. Kinsbourne opined that A.F.M. had an "absence seizure," and that absence seizures generally last a few seconds and no longer than 30 seconds. Pet. Ex. 37 at 3. In his third report, he opined that A.F.M.'s first seizure was 41 minutes in duration, based on his interpretation of the EMS report. Pet. Ex. 41 at 3. In his third and fifth expert reports, Dr. Kinsbourne opined that A.F.M. had a "prolonged absence seizure [that] exceeded 30 minutes in duration." Pet. Ex. 41 at 1; see also Pet. Ex. 43 at 1. In his fifth report, Dr. Kinsbourne pulled back from his earlier opinion that A.F.M.'s initial seizure was 41 minutes, and instead he opined that A.F.M. was "unresponsive for 30 minutes or more." Pet. Ex. 43 at 1.

### ii. Table Claim

In his first expert report, Dr. Kinsbourne specifically stated that his opinion was "as to causation-in-fact." Pet. Ex. 37 at 6. He did not offer opinions to support a Table claim or suggest that A.F.M. had acute encephalopathy demonstrated by a "significantly decreased level of consciousness that last[ed] at least 24 hours." 42 C.F.R. § 100.3(c)(2)(i)(A)(1). He did not appear to offer any opinions supporting a Table claim thereafter, in his expert reports, or at the hearing.

### iii. Causation-in-Fact

Dr. Kinsbourne opined, "to a reasonable degree of medical probability, that [A.F.M.'s] six-month vaccinations, most likely the DTaP, caused [her] epilepsy, leading into epileptic encephalopathy." Pet. Ex. 37 at 6. His specific opinions are set forth below.

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[36] This type of epilepsy is also referred to as migrating partial seizures of infancy ("MPSI"). See Pet. Ex. 41B (Amy McTague et al., Migrating Partial Seizures of Infancy: Expansion of the Electroclinical, Radiological and Pathological Disease Spectrum, 136 Brain 1578 (2013)). In his second expert report, Dr. Kinsbourne referred to A.F.M.'s diagnosis as "malignant migrating partial seizures of infancy (MMPSI)." Pet. Ex. 39 at 2. And in his sixth report, Dr. Kinsbourne referred to AFM's disorder as "migrating focal seizures in infancy (MFSI)." Pet. Ex. 44 at 1. Respondent's expert, Dr. Holmes, referred to A.F.M.'s disorder as "malignant migrating partial seizures of infancy." Resp. Ex. A at 20. He also referred to it as "migrating focal epilepsy," "malignant migrating focal epilepsy," and "multifocal migrating epilepsy." Resp. Ex. F at 4; Resp. Ex. G at 1. The medical literature also uses different names, including "migrating focal seizures in infancy" and "malignant migrating partial seizures in infancy." Pet. Ex. 44a (Robert Horacio Caraballo, Migrating Focal Seizures in Infancy: Analysis of the Electroclinical Patterns in 17 Patients, 23 J. Child Neurology 497 (2008)); Resp. Ex. A, Tab 1 (Giangennaro Coppola, Malignant Migrating Partial Seizures in Infancy: An Epilepsy Syndrome of Unknown Etiology, 50 Epilepsia 49 (2009)). For the sake of simplicity, the undersigned will use the acronym of MFEI (migrating focal epilepsy of infancy) throughout this Decision, unless quoting a medical record, expert report, medical article, or testimony.

### 1. Althen Prong One

At the hearing, Dr. Kinsbourne explained that his opinions were specific to the DTaP vaccine administered on May 7, 2014. Tr. 38. He opined that the DTaP vaccination[37] is known to carry a risk for causing seizures within three days of administration. Tr. 18; see also Pet. Ex. 37 at 4. He posited that the vaccination activates the innate immune system the same way that infection does, leading to the release of proinflammatory cytokines that cause inflammation of the brain. Tr. 18. This leads to overactivity or excitation of neurons, disrupting the balance, and manifesting as seizures. Tr. 18-19. The onset or first seizure "renders the brain more excitable" due to the production of proinflammatory cytokines, and momentum gathers to lead to devasting results. Tr. 22. More specifically, Dr. Kinsbourne opined that the acellular pertussis component of the vaccine led to secretion of proinflammatory cytokines which affect the microglia in the cerebral cortex, which put out more proinflammatory cytokines, which overactivated neurons, causing seizures. Tr. 54.

According to Dr. Kinsbourne, epilepsy is a "hyperexcitability condition" of the brain. Tr. 38. He explained that in the "normal brain, the different neurons are acting differently depending on the circumstances, but if all the neurons . . . fire together, then an epileptic seizure is likely to occur." Tr. 45. The process by which a single afebrile seizure evolves into epilepsy was described by Dr. Kinsbourne as follows: Cytokines lower the seizure threshold, and when the seizure occurs the next time, the threshold lowers, and over time, the brain is modified so that seizures occur without fever or other provocation, which is epilepsy. Tr. 58.

Dr. Kinsbourne conceded that vaccine-related "isolated seizures" can occur that do not cause harm. Tr. 22. But he did not agree that was the case here. Id. He asserted that the first seizure was followed by a second one, with behavioral arrest, followed by a third seizure, where there was also behavioral arrest. Id.

He also discussed his opinions about whether seizures can only occur in the context of fever. Dr. Kinsbourne opined that when seizures occur without fever, they are called afebrile seizures. Tr. 22. He explained that in "special circumstance[s] . . . if the child already has a lower seizure threshold, [] an afebrile seizure is much more likely." Tr. 23. He asserted that vaccines lower the seizure threshold and release the inherent tendency in a child with a genetic susceptibility. Tr. 24-25. And he testified that this process could occur in the absence of fever. Tr. 23; see also Pet. Ex. 39 at 4.

[37] Dr. Kinsbourne acknowledged that use of the acellular pertussis vaccination, as compared to the former whole-cell pertussis vaccine, has "radically reduced the frequency of pertussis-vaccine related seizures," but he asserted that "seizures still occur." Pet. Ex. 37 at 3-4; see also Pet. Ex. 39 at 3.

Dr. Kinsbourne referenced several articles to support his opinions that proinflammatory cytokines can lead to seizures and epilepsy. Tr. 39. Vezzani and Baram[38] explored the mechanisms "that transform a normal brain to an epileptic one," acknowledging that these processes "are not fully understood." Pet. Ex. 37N at 1. They presented "the hypothesis that [the cytokine] IL-1β may contribute to the development of epilepsy" through several pathways. Id. One of these proposed mechanisms is that cytokines "release[d] during the inciting insult may directly contribute to hyperexcitability."[39] Id. The phenomenon of hyperexcitability is "particularly well defined in temporal lobe epilepsy," however this type of epilepsy is not at issue in this case. Id. Further, the authors explained that the "formation of a hyperexcitable circuit may depend on a "functional . . . abnormality in the case of epilepsies involving genetic causes." Id. Lastly, the authors discussed the role of IL-1β in the context of fever and febrile seizures. See id. at 3. Vaccinations were not discussed.

Another paper cited by Dr. Kinsbourne was published by Dr. Holmes and Ben-Ari[40] and stated that "seizures in the developing brain can result in irreversible alterations in neuronal connectivity." Pet. Ex. 37E at 1.[41] The authors explained that the "core physiologic feature of epileptic seizures is hyperexcitability of [central nervous system ("CNS")] neurons. When a sufficient number of neurons synchronously depolarize and generate action potentials, a seizure begins." Id. at 2. Although "children are at higher risk for seizures than adults," the "developing neurons [in children] are less vulnerable [to] neuronal damages and cell loss." Id. at 3. However, "prolonged or recurrent seizure activity . . . can irreversibly alter the way the immature brain develops . . . [and] alterations in normal neuronal connectivity can result in long-term consequences in seizure susceptibility, learning and memory, and risk for subsequent seizure-induced injury." Id. at 5.

Next, Dr. Kinsbourne testified that when infections trigger seizures, they do so by innate immune system activation, which stimulates production of proinflammatory cytokines and lowers the seizure threshold. Tr. 41. He asserted that vaccines trigger the innate immune system in the same way as infections. Tr. 43; Pet. Ex. 37 at 5. Further, he opined that whether a seizure caused by the DTaP vaccination leads to a seizure that "proceeds to epilepsy depends on other

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[38] Annamaria Vezzani & Tallie Z. Baram, New Roles for Interleukin-1 Beta in the Mechanisms of Epilepsy, 7 Current Rev. Basic Sci. 45 (2007).

[39] For further discussion of Dr. Kinsbourne's opinions about inflammation and its effect on excitability and the excitation-inhabitation ratio, see Pet. Ex. 37 at 5.

[40] Gregory L. Holmes & Yehezkiel Ben-Ari, The Neurobiology and Consequences of Epilepsy in the Developing Brain, 49 Pediatric Rsch. 320 (2001).

[41] Dr. Kinsbourne also cited Chen et al., which discussed an animal study suggesting the pertussis toxin can "promote the generation of IL-17 producing CD4 cells through a proinflammatory cytokine pathway." Pet. Ex. 39C at 8 (Xin Chen et al., Pertussis Toxin by Inducing IL-6 Promotes the Generation of IL-17-Producing CD4 Cells, 178 J. Immunology 6123 (2007)). The authors did not discuss the acellular pertussis vaccine at issue here.

factors to do with the patient, not with the vaccination. Some seizures lead to epilepsy; some don't." Tr. 44. Dr. Kinsbourne cited Wang et al.[42] for "insight" as to how "seizures engender seizures." Pet. Ex. 37 at 6 (citing Pet. Ex. 50).

Wang et al. studied the relationship between cytokine levels and severe epilepsy by sampling serum cytokine levels from 1,218 patients with temporal lobe epilepsy, extra-temporal lobe epilepsy, and idiopathic generalized epilepsy. Pet. Ex. 50 at 1, 12.[43] Interictal[44] serum levels of six cytokines, including Il-1β,[45] were "associated with seizure severity" and three cytokines were "significant biomarkers for patients with severe epilepsy." Id. at 12. The authors concluded that "among 14 cytokines, four independent biomarkers (Il-6, IFNγ, IL-17a, and IFNλ3) for severe seizures in three different types of epilepsy were identified." Id. They stated that "[i]mportant roles of these cytokines in the development of severe seizure[s] could be speculated, and they may be used as potential markers to identify severe epilepsy." Id. However, the authors did not conclude that vaccination in general, or the DTaP vaccination specifically, induced cytokine release that caused severe epilepsy.

In further support of his opinions, Dr. Kinsbourne cited a study by Sun et al.[46] examining the risk of febrile seizures and epilepsy after DTaP, IPV, and Hib vaccinations in Denmark. Pet. Ex. 47. Vaccinations were "associated with an increased risk of febrile seizures on the day of the first [two] vaccinations given at [three] and [five] months." Id. However, vaccination "was not associated with an increased risk of epilepsy." Id. Febrile seizures are not at issue here.

On cross-examination, Dr. Kinsbourne conceded that there are no animal models to show that activation of the immune system causes epilepsy. Tr. 38-39.

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[42] Ye Wang et al., Interictal Cytokine Levels Were Correlated to Seizure Severity of Epileptic Patients: A Retrospective Study on 1218 Epileptic Patients, 13 J. Translational Med. 378 (2015).

[43] Dr. Kinsbounre also cited another article which discussed the role of cytokines in epilepsy. See Pet. Ex. 37J (Gang Li et al., Cytokines and Epilepsy, 20 Seizure 249 (2011)) (summarizing three different cytokines and their role in epilepsy).

[44] Interictal refers to "occurring between attacks or paroxysms." Interictal, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=25576 (last visited Oct. 16, 2023).

[45] Only the cytokine Il-6, however, was associated with seizure severity in three types of epilepsy studied. Pet. Ex. 50 at 13.

[46] Yuelian Sun et al., Risk of Febrile Seizures and Epilepsy After Vaccination with Diphtheria, Tetanus, Acellular Pertussis, Inactivated Poliovirus, and Haemophilus Influenzae Type B, 307 JAMA 823 (2012). This is also cited as Resp. Ex. A, Tab 8.

### 2. Althen Prong Two[47]

Dr. Kinsbourne opined that the incident on May 8, 2014 was A.F.M.'s "onset seizure" and that it triggered her epileptic encephalopathy. Tr. 21. A.F.M. had a genetic susceptibility and her vaccinations triggered the onset of her epileptic encephalopathy. Tr. 10. He testified that once epilepsy is set in motion, "it keeps going, [and] the genetic flaw wreaks its devasting effect on the individual's brain." Tr. 21.

He further opined that A.F.M. "suffers from a rare epileptic encephalopathy called migrating focal or partial epilepsy of infancy or MFEI." Tr. 8. Dr. Kinsbourne described MFEI as "a condition in which the cerebral cortex is hyperstimulated, [and] hyperexcitable." Id. "[F]ocal locations in the cortex [] send out paroxysmal waves, which are epileptic." Id. In A.F.M.'s case, there "is an exchange of focal epilepsy from one hemisphere to the other" and back and forth across the cortex. Id. The "focus . . . changes and changes . . . over time." Id. MFEI is "a very serious disorder," and "an epileptic encephalopathy" with "seizures [that] have detrimental effects on the development of the child." Tr. 9. Dr. Kinsbourne opined that the "seizures are so damaging that in some cases the child loses almost all [] prospective skills." Id. He added, it is more than epilepsy, since it is "also a disorder of the brain, which retards development." Id. He further opined that the illness usually appears before six months of age. Id.

At the hearing, Dr. Kinsbourne testified that A.F.M.'s initial seizure was "very consistent" with seizures seen in MFEI. Tr. 13. He opined that the seizure was "focal," characterized by a "state of behavioral interruption," difficulty with breathing, limpness, and an abnormal position. Tr. 12. A.F.M. also had abnormal color, described "both as pallor and . . . looking red." Id. In addition to describing the onset seizure as consistent with MFEI, Dr. Kinsbourne also opined that an appropriate characterization was "hypomotor seizure," a description used by Dr. Holmes.[48] Tr. 13-14. He agreed that A.F.M. was afebrile before the event. See Pet. Ex. 39 at 6; Tr. 53.

Regarding A.F.M.'s diagnosis of MFEI, Dr. Kinsbourne cited Caraballo et al., who described three types of onset in MFEI. Pet. Ex. 44 at 2 (citing Pet. Ex. 44A at 1). Dr. Kinsbourne opined that type two is descriptive of A.F.M.'s seizure type. Id. Type two seizures are "focal complex seizures characterized by behavioral arrest with lip cyanosis and oro-

[47] Some of Dr. Kinsbourne's opinions related to prong two are covered in the section above related to diagnosis and are not repeated here.

[48] Dr. Holmes first used the term "hypomotor seizure" in his sixth expert report. Resp. Ex. G at 4.

alimentary automatism[49] without obvious motor manifestations." Id. (quoting Pet. Ex. 44A at 2, 9). Caraballo et al. described the course of 17 infants with MFEI seizure disorders and explained the EEG features, therapy, and long-term outcome. Pet. Ex. 44A at 1. The mean age of seizure onset was 40 days of age, with a median of 31 days. Id. at 2. Seizures became progressively frequent over a period of 10 to 60 days. Id. In nine patients with type two (as described by Dr. Kinsbourne), the first seizures were "characterized by behavioral arrest, [and] autonomic manifestations (such as apnea, flushing, or cyanosis)." Id.; see also Pet. Ex. 44 at 2. "Soon after onset, the daily seizures became very frequent in all 17 patients, evolving into a status epilepticus in 15." Pet. Ex. 44A at 2. The children were "generally refractory to antiepileptic drugs and [had] severe psychomotor delay . . . before the age of [five] months." Id. at 7. Vaccines were not discussed or identified as a trigger or cause in any of the patients.

Regarding A.F.M.'s EEG findings, Dr. Kinsbourne agreed that A.F.M.'s first EEG (May 13, 2014) was normal, her second EEG was abnormal, and her third EEG clearly showed epileptic encephalopathy. Tr. 17. He opined that the first EEG does not have to be abnormal. Tr. 25; Pet. Ex. 41 at 1. When asked why an EEG would be normal in a child with symptomatic epilepsy, Dr. Kinsbourne opined that experts are unable to explain this finding. Tr. 54.

But in attempts to support his opinion that EEGs may be normal, he again cited Caraballo et al., who described EEG findings in children with MFEI. See Pet. Ex. 42 at 2-3 (citing Pet. Ex. 44A).[50] They described the "characteristic ictal [EEG] pattern consisting of seizures that arise independently and sequentially from both hemispheres[] that are refractory to antiepileptic drugs." Pet. Ex. 44A at 1. The authors also reported that the "interictal EEG at onset showed normal background activity even during sleep in all patients." Id. at 2.

The second article cited by Dr. Kinsbourne about MFEI was authored by McTague et al. which reported on a British study involving 14 children. Pet. Ex. 41B at 1. The authors described the condition as a "rare early infantile epileptic encephalopathy with poor prognosis, presenting with focal seizures in the first year of life." Id. Most of the infants had focal seizures that "were clearly migratory in [eight] of 14 cases." Id. at 4. Some infants had "aversive seizures with head turning and involvement of the eyes with eye flickering or rolling." Id. Most had facial flushing followed by drooling or pupil changes. Id. Frequent seizures occurred in 14 patients. Id. McTague et al. observed 14 children with the condition and noted that the initial EEG was normal in three out of the 14. Id. at 5. But by six months, most infants were abnormal, showing "diffuse background slowing and multifocal epileptogenic foci." Id. The cause was attributable to "multiple genetic, structural[,] and metabolic causes similar to that seen in other

[49] Automatisms "refer to purposeful or quasipurposeful movements that occur without the patients' awareness and with subsequent amnesia concerning the episode." Resp. Ex. A, Tab 12 at 3 (G.L. Holmes, Absence (Petit Mal) Seizures, in Diagnosis and Management of Seizures in Children 173 (1987) (also cited as Resp. Ex. F, Tab 11)). For example, automatic behavior may consist of licking the lips, chewing, grimacing, etc. Id.

[50] Dr. Kinsbourne also referenced articles about Dravet syndrome, that reported infants with this condition may have normal EEGs early in the clinical course. See Pet. Ex. 42 at 2-3.

early infantile epileptic encephalopathy syndromes." Id. at 12. Vaccines were not discussed or identified as playing a role in causation.

Further, Dr. Kinsbourne explained that EEGs are done in the "quiet period" between seizures, called the interictal period. Tr. 55. He concluded that while an interictal EEG is often abnormal in epilepsy, it is not always abnormal. Id.

Moving to the progression of A.F.M.'s seizure disorder, Dr. Kinsbourne explained how the event on May 8, 2014 caused A.F.M.'s subsequently diagnosed seizure disorder. He opined that the seizure on May 8 "initiated an innate immune reaction that through the action of proinflammatory cytokines lowered the seizure threshold." Pet. Ex. 44 at 2. "[I]f the child's seizure threshold [had] already been lowered by a genetic abnormality," he opined that "even a usually harmless proinflammatory response can suffice to lower seizure threshold even further, to the point at which a triggered seizure occurs." Id. at 3.

Dr. Kinsbourne acknowledged that the cause of A.F.M.'s epilepsy is genetic. Tr. 9; Pet. Ex. 44 at 1.[51] "Although A.F.M.'s underlying genetic susceptibility . . . has not been identified, it is clear from the medical literature that she must harbor a severe underlying genetic flaw." Pet. Ex. 44 at 1. There is "no one particular genetic flaw" that causes the disorder, and the genetic basis is not yet known. Tr. 9. According to Dr. Kinsbourne, A.F.M. had a "very serious susceptibility, which was inherited" and present from birth, and "the vaccination [] triggered the onset of its clinical manifestations." Id. "In the absence of such a genetic predisposing factor, A.F.M. would most likely have developed quite normally, vaccination or not." Pet. Ex. 44 at 1.

Although Dr. Kinsbourne recognized the genetic etiology of A.F.M.'s epilepsy, he opined that A.F.M.'s vaccination "was the trigger that launched the clinical onset" of her seizure disorder. Pet. Ex. 44 at 1. As explained by Dr. Kinsbourne, A.F.M.'s underlying genetic abnormality acted to reduce her seizure threshold, and so her seizures occurred even without the presence of a fever. Id.; Tr. 23-24. He testified that "[a]ll vaccines do is to lower the seizure threshold." Tr. 24. He further opined vaccines "don't cause a disease like A.F.M. has. It was inherent in her, and . . . [vaccines] released it." Tr. 24-25. Dr. Kinsbourne opined that on May 8, A.F.M. did not have a fever, and therefore, her seizure would be classified as afebrile. Tr. 53. Also, since she did not have a fever, Dr. Kinsbourne conceded there was no evidence that A.F.M. had inflammatory cytokines, other than the fact that she had seizures. Tr. 60-61.

After acknowledging that MFEI is associated with genetic abnormalities, Dr. Kinsbourne reviewed several articles that discussed the prognosis of children with this type of epilepsy. He concluded that if A.F.M. had not received the vaccination at issue, she "would have had the

[51] In his second expert report, Dr. Kinsbourne opined that A.F.M. did "not necessarily" have a genetic cause for her seizures." Pet. Ex. 39 at 4. But if she did, he agreed that it "might explain her susceptibility to epileptogenesis," but "it would not counteract the fact," that he believed her vaccination triggered her "onset seizure." Id. In a subsequent expert report, however, Dr. Kinsbourne acknowledged that migrating focal epilepsies have been associated with several different genetic abnormalities, including SCN2A variants. See Pet. Ex. 42 at 3.

benefit of a longer period of uninterrupted psychomotor development before the onset of her epilepsy had it not been triggered by vaccinations." Pet. Ex. 42 at 4. He concluded that the vaccinations "deprived her of the chance to achieve further normal mental development pending any ultimate seizure onset." Id. But at the hearing, Dr. Kinsbourne took the position that if A.F.M. had not been vaccinated, her condition might not have been triggered or might "not have been as severe." Tr. 26. But he agreed that most children who have migrating focal epilepsy of infancy are "severely damaged." Id. And he agreed that A.F.M. had a severe course consistent with most children. Id.[52]

He cited animal studies on SCN1A mutation seizure disorders to support his opinion that genetic abnormalities make a child "more susceptible than normal to the detrimental effects of the seizures." Pet. Ex. 43 at 2. But he disagreed with the methodology and statistical analysis of studies[53] that purported to conclude that earlier seizure onset (in the context of the SCNIA genetic mutation) in children with vaccine proximate seizures did not affect outcome. Id. at 3. He argued that there is "no evidence to support the view that developmental history is unrelated to the age at seizure onset." Id. at 4. He cited several papers to support his opinion that age at seizure onset could affect outcome.

The first paper was by Dutton et al.[54] Pet. Ex. 43B. The animal studies reported by Dutton et al. examined two models of complex early-life febrile seizures in a mouse line that expressed a SCN1A mutation to examinate the role of complex febrile seizures in "long-term disease progression." Id. at 10. The first model induced prolonged febrile seizures and the second induced acute febrile seizures followed the next day by an induced prolonged febrile seizure. Id. The research showed that "complex early-life [febrile seizures] lead to increased seizure susceptibility, more severe spontaneous seizures," impairments in behavior and memory, and more severe adult SCN1A epilepsy. Id. The results, however, were limited to febrile seizures and their effects on adults with epilepsy with the SCN1A mutations. The authors did not discuss a model characterized by only one afebrile seizure.

[52] Dr. Kinsbourne argued that MFEI does not always result in "severe intellectual disability." Pet. Ex. 42 at 3. He opined that developmental outcome is "attributable to the cumulative impact of the seizures once they begin." Id.

[53] Specifically, Dr. Kinsbourne disagreed with McIntosh et al., who determined that while vaccination "might trigger earlier onset of Dravet syndrome in children who, because of an SCN1A mutation, are destined to develop the disease," but found "no evidence that vaccinations before or after disease onset affect[ed] outcome." Pet. Ex. 42G at 1 (Anne M. McIntosh et al., Effects of Vaccination on Onset and Outcome of Dravet Syndrome: a Retrospective Study, 9 Lance Neurology 592 (2020)). This is also cited as Resp. Ex. G, Tab 12.

[54] Stacey B.B. Dutton et al., Early-Life Febrile Seizures Worsen Adult Phenotypes in SCN1A Mutants, 293 Experimental Neurology 159 (2017).

The second article cited by Dr. Kinsbourne, by Salgueiro-Pereira et al.[55] reported on an animal study done on mice carrying an SCN1A mutation where short seizures were induced daily for 10 days using hyperthermia or a chemical that induces seizures (Flurothyl.) Pet. Ex. 43H at 2. The research demonstrated that the mice with an asymptomatic or mild phenotype were transformed into a "severe [Dravet syndrome-like] phenotype," with increased seizures and "cognitive/behavior deficits." Id. The authors did not study the effects of one afebrile seizure.

Moreover, Dr. Kinsbourne recognized the speculative nature of hypothetical "what if" questions about what would have happened if A.F.M. had not received her DTaP vaccination. See Tr. 26. He stated, "[t]he whole point is that we don't know what would have happened if the vaccination hadn't been given and the disease hadn't been triggered." Id.

### 3. Althen Prong Three

Dr. Kinsbourne opined that A.F.M.'s condition began "16 hours after the vaccinations" which "places the situation in the . . . risk period of seizure onset after DTaP." Tr. 11. Dr. Kinsbourne opined that the risk period of seizures with DTaP is the first three days after vaccination, although the first day and earlier is most notable. Tr. 18. A.F.M. had her seizure at approximately 16 to 17 hours after her DTaP vaccination, which is within the known risk period. Tr. 26-27. He further opined that the vaccination given on May 7, 2018 triggered A.F.M.'s "epileptic encephalopathy." Tr. 10.

## 2. Respondent's Expert, Dr. Gregory Lawrence Holmes[56]

### a. Background and Qualifications

Dr. Holmes earned his B.S. from Washington and Lee University in 1970, and his M.D. from University of Virginia School of Medicine in 1974. Resp. Ex. H at 1. He is a licensed physician with board certifications in pediatrics, neurology, and neurophysiology. Id.; Resp. Ex. A at 1; Tr. 72. Dr. Holmes is currently a Professor of Neurological Sciences and Pediatrics and Chair of the Department of Neurological Sciences at the University of Vermont College of Medicine. Resp. Ex. A at 1; Resp. Ex. H. at 1-2; Tr. 73. As Chair of the Department, he is responsible for the physicians, the research, and the educators, and is heavily involved in clinical care. Tr. 73-75. Dr. Holmes mainly sees patients of pediatric neurological disorders. Tr. 74. His primary research interest is epilepsy. Tr. 80. Dr. Holmes has authored numerous

[55] Ana Rita Salgueiro-Pereira et al., A Two-Hit Story: Seizures and Genetic Mutation Interaction Sets Phenotype Severity in SCN1A Epilepsies, 125 Neurobiology Disease 31 (2019).

[56] Dr. Holmes submitted six expert reports and testified at the entitlement hearing on May 17, 2022. Resp. Exs. A, C-G; Tr. 3.

publications, including a number of medical articles that have been filed here.[57] See Resp. Ex. H at 36-82; Tr. 82-83. He has reviewed a number of cases and testified in the Vaccine Program many times but has never found a vaccine-related injury. Tr. 150-51.

**b. Opinions**

Like Dr. Kinsbourne, Dr. Holmes offered opinions about what happened to A.F.M. on May 8, as well as causation.

**i. Initial Event May 8, 2014—Seizure vs. ALTE**

Dr. Holmes opined that A.F.M.'s event on May 8, 2014 was an "apparent life-threatening event" or ALTE. Tr. 94. He agreed with the characterization of an ALTE described by Aminiahidashti. Resp. Ex. F at 3. Dr. Holmes noted that ALTE is a "concern in the neonatal period" up to the first year of life, including the age of A.F.M. at the time of her initial event. Id. Aminiahidashti described ALTE as "an episode that is frightening to the observer, and is characterized by some combination of apnea, color change, marked change in muscle tone, choking, gagging, or coughing." Pet. Ex. 42A at 1. The underlying cause "varies." Id. at 2. "The most frequent problems associated with ALTE are gastrointestinal (50%), neurologic (30%), respiratory (20%), cardiovascular (5%), metabolic and endocrine (<5%), or others." Id.

One reason for Dr. Holmes' opinion included the medical record noting that A.F.M. had "some degree of apnea," her color was "pallid," she was "very limp and hypotonic," and when suctioned, she had "a lot of saliva and mucus." Tr. 95. When asked to respond to Dr. Kinsbourne's opinion that A.F.M. had a seizure, Dr. Holmes opined that it was "very, very difficult based on the medical records to be so definitive" as to conclude that A.F.M. had a seizure. Id. Instead of a seizure, Dr. Holmes believed it was more likely that A.F.M. had reflux, a vasovagal attack, or laryngospasm, causing choking and decrease blood flow to the brain. Tr. 98. He agreed that ALTE encompassed seizure activity. Tr. 141. Dr. Holmes also acknowledged that A.F.M. was afebrile before the event. See Resp. Ex. A at 21; Tr. 126, 180.

Although Dr. Holmes opined that A.F.M. had an ALTE on May 8, he agreed that the EMS providers who transported A.F.M. to the hospital thought that she had a seizure. Tr. 140

[57] See Pet. Exs. 37E, 37F (Gregory L. Holmes & Pierre-Pascal Lenck-Santini, Role of Interictal Epileptiorm Abnormalities in Cognitive Impairment, 8 Epilepsy & Behavior 504 (2006)); Resp. Ex. A, Tabs 12, 16, 28 (Gregory L. Holmes, Seizure-Induced Damage in the Developing Human: Relevance of Experimental Models, in 135 Progress in Brain Research 321 (T. Situla & A. Pitkanen eds., 2002)); Resp. Ex. F, Tab 14 (Gregory L. Holmes et al., Maturation of EEG Oscillations in Children with Sodium Channel Mutations, 34 Brain & Development 469 (2012) (also cited as Resp. Ex. G, Tab 17)).

(citing Pet. Ex. 38 at 2). During the hearing, after reviewing the EMS trip report,[58] Dr. Holmes agreed A.F.M.'s respirations were noted to be irregular, and that this could be consistent with a seizure. Tr. 154. He also acknowledged that A.F.M.'s pupils were described as dilated and her eyes rolled back, and these abnormalities can be seen with seizures. Tr. 154-55. Even after reviewing the EMS report, however, Dr. Holmes remained skeptical that A.F.M. had a seizure. Tr. 165.

Dr. Holmes noted that the ED physician's (Dr. Ervin's) impression was "6-month-old with an [URI]; episode of altered mental status, suspect possibly secondary to a reflux or a choking episode, but she did not have any cyanosis; and a possible [UTI]." Resp. Ex. E at 1 (citing Pet. Ex. 7 at 22). A.F.M. was admitted for observation; antibiotics and intravenous fluids were administered, and medication for congestion was ordered. Id. Dr. Holmes observed that Dr. Ervin did not diagnose a seizure. Id.

According to Dr. Holmes, ALTE "is a basket-term," to describe events when there is insufficient information upon which to discern a specific diagnosis. Tr. 96. In contrast, he testified the diagnosis of a seizure requires enough information so that it can be classified using the International Classification of Seizures in Epilepsy (most recently updated in 2017).[59] Id.

Regarding the fact that A.F.M.'s initial EEG was normal, Dr. Holmes agreed with Dr. Kinsbourne that "a normal EEG or MRI does not rule out the possibility of a seizure." Resp. Ex. D at 1. He further opined that an "EEG [] done six days after the event on May 8 [] cannot be used to determine if the [] event was a seizure." Id. If the EEG had been abnormal, and shown epileptiform activity, Dr. Holmes opined then it would have been more likely that A.F.M.'s initial event was a seizure. Id.

On cross-examination, Dr. Holmes was asked questions about a note written by Dr. Terayanont documenting a history of A.F.M.'s illness after she was admitted to the hospital for seizure activity on June 22, 2014. See Tr. 168. Dr. Terayanont took a history from Petitioner and her mother who reported that the event on June 22 was "the third time" that she had "this particular symptom." Pet. Ex. 9 at 7. The "symptoms started with eye staring and eventually eyes rolled to the left and [she had] slightly jerking movement of both upper extremities which last[ed] for about a few seconds. There is no history of cyanotic spell" and "the patient

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[58] Chief complaint was "possible seizure like activity." Pet. Ex. 38 at 1. A.F.M. was found "unresponsive; respirations irregular and labored; lung sound clear; pulse reg[ular]; skin pale; pupils dilated non reactive." Id. at 2. A.F.M. was found "with arms extended out; eyes rolled back; not breathing; skin color was normal." Id. A.F.M.'s condition gradually improved throughout the duration of the trip. Id.; see also Pet. Ex. 8 at 53 (ED noted indicating A.F.M. "arrived per EMS with report of suspected seizure activity").

[59] It does not appear that Dr. Holmes filed a reference or provided a citation for this text. He did, however, file an article on the definition and classification of status epilepticus. See Resp. Ex. D, Tab 2 (Eugen Trinka et al., A Definition and Classification of Status Epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus, 56 Epilepsia 1515 (2015)).

recover[ed] by herself." Id. After reviewing this note, Dr. Holmes still disagreed that there was sufficient evidence to conclude that A.F.M. had a seizure on May 8 (which would have been the first time A.F.M. had the symptoms reported to Dr. Terayanont as documented). Tr. 168-69.

While Dr. Holmes did not agree that A.F.M. had a seizure, he did agree that she had an altered state of consciousness during the event. Tr. 143. Based on the times documented in the ambulance trip report, Dr. Holmes opined that A.F.M. was unresponsive for approximately 16 to 20 minutes. Tr. 157-58.[60]

**1. Type and Duration of Event on May 8, 2014**

While Dr. Holmes disagreed that A.F.M. has a seizure, regarding seizure type, Dr. Holmes strongly disagreed with Dr. Kinsbourne's opinion that A.F.M. had an absence seizure[61] or absence status epilepticus[62] on May 8, 2014. Tr. 99-100; Resp. Ex. G at 1. He defined an absence seizure as a "generalized seizure[] [that] involve[s] widespread areas of the brain from the onset." Resp. Ex. D at 2. Further, he explained that absence seizures are "common in children and typically don't cause long term problems." Resp. Ex. A at 21. Dr. Holmes also noted that absence seizures usually occur in older children, ages four to 14 years. Id. Lastly, he opined that a normal EEG in a child with a suspected absence seizure is "extremely unusual and almost rules out typical absence seizures." Resp. Ex. G at 2 (citing Resp. Ex. G, Tab 5 at 3-4, 7-8, 14 (explaining that typical and atypical absences seizures are characterized by abnormal EEGs and "[a] normal EEG in a young child with recent appearance of suspect absences is extremely unusual and almost rules out typical absences if adequate hyperventilation[63] was performed").[64]

He further explained that absence status epilepticus is "very rare" and "typically seen in adolescents." Resp. Ex. F at 1. Moreover, this type of seizure usually occurs in patients with

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[60] Dr. Holmes testified that the record reflects a period of 16 minutes, but he noted that this did not account for the time it took for the family to place the call. Tr. 158.

[61] For a more detailed explanation of the reasons that Dr. Holmes disagreed that A.F.M. had absence seizures, see Resp. Ex. A at 21; Resp. Ex. F at 2. Dr. Holmes authored an article on absence seizures in children. See Resp. Ex. A, Tab 16 (Gregory L. Holmes et al., Absence Seizures in Children: Clinical and Electroencephalographic Features, 21 Annals Neurology 268 (1982) (also cited as Resp. Ex. F, Tab 12; Resp. Ex. G, Tab 1)).

[62] For a more detailed explanation of the reasons that Dr. Holmes disagreed that A.F.M. had absence status epilepticus, see Resp. Ex. F at 1.

[63] According to Dr. Holmes, hyperventilation was not performed on A.F.M. due to her age, but she was asleep during her first EEG, and he opined that "sleep is a powerful activator of epileptiform discharges in epilepsy, including absence epilepsy." Resp. Ex. G at 2.

[64] Jean Aicardi, Epilepsy in Children, in 2 The International Review of Child Neurology (Isabelle Rapin ed., 1994).

"idiopathic generalized epilepsy and has an excellent prognosis" and "absence status epilepticus has not been shown to occur in the first year of life." Id. Dr. Holmes further disagreed with Dr. Kinsbourne that the paper by Grin and DiMario supported the idea that A.F.M. had absence status epilepticus. Resp. Ex. G at 2 (citing Pet. Ex. 43E). There the patient had a "long episode of a flat affect, decreased but not absent speech, confusion, and an EEG showing generalized spike and wave activity." Id. (citing Pet. Ex. 43E). A.F.M. did not have a similar presentation, thus Dr. Holmes opined the description "does not fit" what happened here.[65] Id.

If A.F.M. had either an absence seizure or absence status epilepticus, Dr. Holmes testified it would have been very unlikely that her initial EEG (done May 13, 2014) would have been normal. Tr. 100. Also, one week after her event, when seen by her physician on May 15, A.F.M. was described as doing well, and her motor skills were good. Tr. 102. Therefore, Dr. Holmes opined there is "no basis whatsoever" to conclude that A.F.M. had status epilepticus on May 8. Tr. 100. Further, once A.F.M. was diagnosed with epilepsy, Dr. Holmes noted that her seizures were not unusual. Tr. 101. She became "rigid, [with] eye deviation, [and] stiffening of the body." Id. For these reasons, Dr. Holmes concluded that A.F.M.'s event on May 8, 2014, was not an absence seizure or absence status epilepticus. Id.; see also Resp. Ex. G at 2.

Dr. Holmes also disagreed with Dr. Kinsbourne's opinion that A.F.M.'s initial event was a NCSE. Resp. Ex. C at 1; Resp. Ex. D at 2; Resp. Ex. F at 2. He defined NCSE as "a change in mental status from baseline of at least 30-minute duration without convulsive activity, associated with continuous or near continuous EEG ictal discharges that consist of generalized or focal spikes, spike-waves or slow activity with intermixed spikes." Resp. Ex. D at 2 (citing Resp. Ex. F, Tab 13 at 3-4).[66] He opined that NCSE is associated with "severe brain insults, such as hypoxia,[67] intracranial hemorrhage, [and] with abnormal MRI scans." Resp. Ex. C at 1. Dr. Holmes explained that it is "implausible that A.F.M. had NCSE and awoke in the ambulance, arriving in the [ED] alert and playful." Id. Moreover, he noted that none of the treating physicians considered NCSE as a possible diagnosis. Id. Dr. Holmes also opined that if

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[65] In the case report, the exact length of time the patient was disoriented was not noted. However, she was disoriented and confused upon awakening, and returned to bed, and fell asleep for one hour. Pet. Ex. 43E at 1-2. When she awoke, she was coherent, but later enroute to the hospital, she became confused again. Id.

[66] Stacey K.H. Tay et al., Nonconvulsive Status Epilepticus in Children: Clinical and EEG Characteristics, 47 Epilepsia 1504 (2006). The patients studied by Tay et al. had EEG abnormalities ranging from "typical and atypical spike and wave discharges" to "multiple or polyspike discharges and rhythmic sharp delta activity with evolution." Resp. Ex. F, Tab 13 at 3. "Interictal abnormalities were present in all the patients in EEGs obtain after the resolution of NCSE." Id. at 4.

[67] Hypoxia is the "reduction of oxygen supply to tissue below physiologic levels despite adequate perfusion of the tissue by blood." Hypoxia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=24462 (last visited Oct. 16, 2023).

A.F.M.'s initial seizure had been NCSE, her initial EEG would likely have been abnormal. Resp. Ex. D at 1; Resp. Ex. F at 2.

When asked to assume hypothetically that A.F.M.'s event was a seizure, and asked to describe the seizure type, Dr. Holmes testified that he would have categorized it as a "hypomotor seizure." Tr. 97. He defined hypomotor seizures as those "characterized by decreased behavior activity with indeterminate level of consciousness." Resp. Ex. G at 4.[68] He opined that the "majority of hypomotor seizures are partial (focal) in nature, rather than generalized" and the "focal EEG abnormalit[ies] . . . usually involve the temporal or temporoparietal brain regions resulting in a diminution of behavioral motor activity." Id. As it relates to A.F.M., however, characterizing A.F.M.'s initial event as a hypomotor seizure was not satisfactory to Dr. Holmes because A.F.M. was described as limp, and he has never seen a seizure "documented with EEG in which the child was totally limp and floppy." Tr. 98.

### ii. Table Claim

Dr. Holmes opined that A.F.M. did not suffer vaccine-induced epileptic encephalopathy. These opinions are integrated below.

### iii. Causation-in-Fact

#### 1. Althen Prong One

Dr. Holmes opined that Dr. Kinsbourne's mechanistic opinion is not reliable. Tr. 110. Specifically, Dr. Holmes disagreed that "a single vaccine given in the thigh [could produce] enough cytokines to lead to seizure" or "irreparable changes in the brain that lead [] to epilepsy," when there is "no evidence of inflammation in the brain." Id. There was no fever, no "abnormal neurological signs," no "alteration in consciousness," no encephalopathy, a normal EEG, and a normal MRI. Id.[69] Given these facts, Dr. Holmes opined the May 8, 2014 event did not cause a "vaccine-induced epileptic encephalopathy." Id.

As explained by Dr. Holmes, the support that the DTaP vaccination can cause an afebrile seizure is very weak. Tr. 112. He noted that the articles cited by Dr. Kinsbourne do not support the idea that there is an increased risk of afebrile seizures after the DTaP vaccination. See id. For example, Conrad and Jensen[70] concluded "that the risk of seizures is lower with the acellular pertussis than the whole-cell pertussis." Resp. Ex. A at 21 (citing Pet. Ex. 37D at 5 (Table 4

[68] For Dr. Holmes' complete description of hypomotor seizures, see Resp. Ex. G at 4.

[69] Dr. Holmes also testified that an MRI would show inflammation if the vaccinations increased cytokines in the brain. Tr. 149-50.

[70] Dennis A. Conrad & Hal B. Jenson, Using Acellular Pertussis Vaccines for Childhood Immunization Potential Benefits Far Outweigh Potential Risks, 105 Postgraduate Med. 165 (1999). This is also cited as Resp. Ex. A, Tab 19.

shows the incidence of fever, and Table 5 shows the estimated rates of moderate to severe adverse reactions of diphtheria-tetanus-pertussis ("DTP") as compared with DTaP, and vastly reduced rates of seizures, particularly for two types of vaccines, Certiva and Tripedia)). Moreover, Dr. Holmes testified that the study published by Le Saux et al.,[71] cited by Dr. Kinsbourne, did not show an increased risk of afebrile seizures after vaccination with DTaP. Id. (citing Pet. Ex. 37I at 1, 4-5 (noting "risks of febrile seizures and [hypotonic-hyporesponsive episodes] . . . declined significantly with the introduction of acellular pertussis vaccine")).

Regarding Dr. Kinsbourne's reliance on the paper by Chen et al., Dr. Holmes noted that it was a study about the pertussis toxin and not the pertussis vaccination and its effect on the proinflammatory cytokine pathway. Resp. Ex. C at 2 (citing Pet. Ex. 39C). Additionally, Dr. Holmes cited Sun et al., which evaluated febrile seizures after childhood vaccinations (including DTaP) given at three, five, and 12 months, and found that while the vaccinations were "associated with an increased risk of febrile seizures on the day of the first [two] vaccinations given at 3 and 5 months," that "vaccination with DTaP-IPV-Hib was not associated with an increased risk of epilepsy." Tr. 122 (citing Pet. Ex. 47 at 1).

Dr. Holmes opined that there is a condition characterized by afebrile seizures, but it is related to a specific epileptic syndrome, Dravet syndrome. Tr. 112. He explained that some studies have shown that some children with Dravet syndrome have seizures after the DTaP vaccination, but studies have also shown the post-vaccination seizure does not alter the child's course. Tr. 113-16; Resp. Ex. F at 3-4; see Resp. Ex. G, Tab 12; Pet. Ex. 37M at 10.[72]

In support of his opinion regarding the role of genetics in the etiology of epilepsy, Dr. Holmes cited a study by Verbeek et al. (also cited by Dr. Kinsbourne), of 990 children who had seizures after vaccination within the first two years. Tr. 117 (citing Pet. Ex. 37M at 1). The study showed that "in most cases genetic or structural defects [were] the underlying cause of epilepsy with onset after vaccination." Id. (citing Pet. Ex. 37M at 1, 10). Dr. Holmes emphasized that vaccination is not the cause of the epilepsy, but the genetic defect is the cause. Id. Similarly, he explained that the article cited by Dr. Kinsbourne, authored by von Spiczak et al.,[73] does not provide evidence that vaccines are the cause of seizures; instead, the underlying cause of the epilepsy is the reason for seizures. Tr. 118 (citing Pet. Ex. 39L).

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[71] Nicole Le Saux et al., Decrease in Hospital Admissions for Febrile Seizures and Reports of Hypotonic-Hyporesponsive Episodes Presenting to Hospital Emergency Departments Since Switching to Acellular Pertussis Vaccine in Canada: A Report From IMPACT, 112 Pediatrics e348 (2003). This is also cited as Resp. Ex. A, Tab 20.

[72] Nienke E. Verbeek et al., Etiologies for Seizures Around the Time of Vaccination, 134 Pediatrics 658 (2014). This is also cited as Resp. Ex. A, Tab 22.

[73] Sarah von Spiczak, A Retrospective Population-Based Study on Seizures Related to Childhood Vaccination, 52 Epilepsia 1506 (2011).

von Spiczak et al. studied seizure types and epilepsy syndromes in infants who presented with seizures after vaccination. Pet. Ex. 39L at 1. They identified clinical information and genetic factors related to Dravet syndrome, West syndrome, as well as other seizure types and syndromes that occurred in temporal association with vaccination. Id. at 11. They concluded that "severe childhood epilepsies comprise a notable subset of these cases," and recommended genetic counseling and "early diagnosis by clinical recognition and confirmation of the underlying etiology." Id.

Dr. Holmes then turned to the issue of whether a single afebrile seizure can cause excitatory changes in the brain that then leads to epileptic encephalopathy, as proposed by Dr. Kinsbourne. Tr. 118. Dr. Holmes strongly disagreed that a single afebrile seizure could cause epileptic encephalopathy. Id. While he did agree that after many seizures, "the brain can become more excitable," he opined that one cannot "equate excitability with epilepsy." Id. He also disagreed that the article he co-authored with Dr. Ben-Ari, proposed that "changes in excitability lead to epilepsy." Tr. 134. The authors explained that "the immature brain is more prone to seizures than the mature brain because of a developmental mismatch between the delicate balance of excitation and inhibition." Resp. Ex. A, Tab 26, at 5. Nothing in the article suggests that a single afebrile seizure can cause epilepsy, instead, "prolonged or recurrent seizure activity, through activity-dependent mechanisms, can irreversibly alter the way the immature brain develops and forms synapses. There alteration in normal neuronal connectivity can result in long-term consequences in seizure susceptibility, learning and memory, and risk for subsequent seizure-induced injury." Id. at 5.

Next, Dr. Holmes reviewed additional medical literature referenced by Dr. Kinsbourne and provided opinions about whether it supported vaccine causation. He explained the Li et al. paper discussed the role of cytokines in epilepsy, but Dr. Holmes opined that there was nothing in the paper relevant to vaccinations. Tr. 129-30 (citing Pet. Ex. 37J). Dr. Holmes agreed that "seizures can lead to increased cytokines," but he disagreed that a "single seizure" can increase cytokines so as to cause epilepsy. Tr. 130. He had similar comments about the Wang et al. paper, regarding the question of whether higher cytokine levels are present in those with frequent seizures and more severe epilepsy. Tr. 137 (citing Pet. Ex. 50). He noted Wang et al. did not relate to vaccination. Id. Likewise, he testified that the article by Braun et al.[74] did not provide evidence that the acellular pertussis vaccine (DTaP) caused epilepsy. Tr. 129 (citing Pet. Ex. 37A).

Dr. Holmes also discussed the Vezzani and Baram papers and agreed that they showed that cytokines in the brain "can be associated with seizures and can be a result of seizures." Tr. 130 (citing Pet. Exs. 37N, 39K). But he explained that they "had not studied vaccines," and specifically vaccines administered peripherally, to determine if they increase the production of

[74] M. Miles Braun et al., Infant Immunization with Acellular Pertussis Vaccines in the United States: Assessment of the First Two Years' Data From the Vaccine Adverse Event Reporting System (VAERS), 106 Pediatrics e51 (2000).

cytokines, or if so, whether this leads to epilepsy. Tr. 130 (citing Pet. Ex. 39K;[75] Pet. Ex. 37N). While he agreed that cytokines "play a role in epilepsy," he opined it is too simplistic to focus only on cytokines when there are other factors that play a role in epileptogenesis. Id. In summary, Dr. Holmes testified that none of the articles about the acellular pertussis vaccine reported a causal association between the vaccine and seizures or epileptic encephalopathy. Tr. 135.

Finally, regarding Dr. Kinsbourne's opinion that a child with MFEI can have a normal EEG, Dr. Holmes agreed. Tr. 123. By way of example, Dr. Holmes opined that children with Dravet syndrome may initially have a normal EEG, but he explained that this is in the context of genetic epilepsy. Id. Dr. Holmes disagreed that the mechanistic theory proposed by Dr. Kinsbourne, resulting in "an encephalopathic process due to cytokines in the brain," would result in a normal EEG. Tr. 124. He explained that if there were sufficient cytokines to result in inflammation in the brain, there should be functional and/or EEG abnormalities. Id.

### 2. Althen Prong Two

Dr. Holmes opined that the vaccination at issue did not play a role in A.F.M.'s neurological condition. Tr. 110. He testified that there is no evidence that A.F.M.'s epilepsy is related to her vaccination. Id. Instead, it "is related to her genetic defect." Id. Moreover, he opined that the vaccination did not cause A.F.M.'s event on May 8, which he opined was not a seizure, but an ALTE. Tr. 111.

Further, Dr. Holmes opined that there was not a logical sequence of cause and effect between vaccination and A.F.M.'s epilepsy. Tr. 125. There was no evidence of an inflammatory response to the DTaP vaccination. Id. He agreed she was afebrile before the event. See Resp. Ex. A at 21; Tr. 126, 180. Dr. Holmes explained that A.F.M. did not have encephalitis[76] or meningitis,[77] or alterations in awareness, alertness, or behavior. Tr. 125. When A.F.M. was seen on May 8, 2014 after the event, she "respond[ed] normally" except for "congestion which had begun a week prior to immunizations." Resp. Ex. A at 20. Dr. Holmes stated that she was diagnosed with an URI, treated with antibiotic, and discharged home.[78] Id. She had no weakness, sleep disturbance, or fever. Tr. 125-26. She had a normal EEG and normal

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[75] Annamaria Vezzani et al., The Role of Inflammation in Epilepsy, 7 Nat'l Rev. Neurology 31 (2011).

[76] Encephalitis is the "inflammation of the brain." Encephalitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=16168 (last visited Oct. 16, 2023).

[77] Meningitis is the "inflammation of the meninges, usually by either a bacterium . . . or a virus." Meningitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=30340 (last visited Oct. 16, 2023).

[78] Dr. Holmes testified that A.F.M.'s infection was not significant to his opinions. Tr. 180.

neurological examination on May 13th, several days after the event. Id. Her MRI was also normal. Id. Based on all these facts, Dr. Holmes testified that it was "inconceivable" that A.F.M. had inflammation of the brain. Tr. 126; see also Resp. Ex. A at 20 (opining that there is no evidence that any injury occurred following A.F.M.'s vaccinations on May 7, 2014).

Conversely, Dr. Holmes opined that on June 22, 2014, A.F.M. did have a seizure.[79] Tr. 103; Resp. Ex. D at 1. She was "rigid and fixed to the right" when she arrived at the hospital and required diazepam intravenously. Tr. 103. Dr. Holmes characterized the event as a "focal seizure with secondary generalization." Tr. 173. An EEG done the next day, June 23, 2014, confirmed "focal seizures [] with secondary generalization." Tr. 104. The EEG findings were consistent with "epileptic interictal discharges involving both hemispheres." Tr. 105. Based on A.F.M.'s seizure on June 22, and her EEG results on June 23, Dr. Holmes agreed that the diagnosis of epilepsy was appropriate. Tr. 167.

After she was diagnosed with epilepsy, Dr. Holmes briefly described A.F.M.'s subsequent course. See Tr. 106-09. On June 29, 2014, video EEG showed a 25-minute seizure and a four-minute tonic-clonic seizure with oxygen desaturation. Tr. 106-07. EEG monitoring from June 30 to July 1, 2014 was markedly abnormal, showing many seizures. Tr. 107. From July 5 to September 12, 2014, A.F.M. was hospitalized at Vanderbilt Hospital. Id. She had a seizure that lasted 140 minutes and required a phenobarbital coma. Id. After that, A.F.M. had an abnormal MRI and clinical deterioration. Tr. 108. Her seizures were very refractory to medication. Id. Dr. Holmes concluded that A.F.M. had a course of continued seizures and cognitive decline. Tr. 109.

Regarding the type of seizures A.F.M. developed in June 2014, Dr. Holmes opined that A.F.M.'s seizure disorder (MFEI) is "a rare, age-specific epileptic encephalopathy." Resp. Ex. A at 20. He explained that onset of the illness occurs by six months of age and is characterized by "frequent multifocal seizures with ictal [EEG] activity shifting from one hemisphere to the other, no identifiable immediate or remote causes, intractability to antiepileptic drugs, profound developmental arrest, hypotonia[,] and often abnormal movements." Id. Although genetic mutations have been found in some patients, other patients do not have identifiable genetic markers. Id.[80] Dr. Holmes believed that A.F.M.'s epilepsy is genetic, although no specific mutation has been identified. Id.

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[79] On May 22, 2014, A.F.M. had another event, described by Dr. Holmes as staring "upward with her mouth open, [and her] face was red." Tr. 103. A.F.M.'s mother reported that her daughter returned to baseline in five minutes. Id. When A.F.M. was seen by Dr. Crick, she was described as "alert, and [in] no acute distress." Id. Dr. Holmes explained that Dr. Crick's assessment was reflux and rule out seizures. Id. Dr. Holmes viewed this second incident as "an usual movement disorder." Tr. 143. He opined that there was not enough information to determine whether A.F.M. had an altered state of consciousness during this second event. Id.

[80] For more details about the genetic mutations that have been associated with A.F.M.'s type of epilepsy, see Resp. Ex. A at 20. Dr. Holmes explained that A.F.M.'s genetic testing "demonstrated a gene variant in SCN4A," but "at this point it is unclear whether the SCN4A mutation has any role in A.F.M.'s current condition." Id.

Dr. Holmes noted that Caraballo et al. and McTague et al., who described MFEI, do not implicate vaccinations as a trigger for seizures or epilepsy. Tr. 132-33 (citing Pet. Exs. 41C, 41B). Dr. Holmes explained that the type of seizures that A.F.M. developed were "quite different than the event on [May 8, 2014]." Id. He also opined that there is no evidence that MFEI is "triggered by vaccination." Id. Lastly, he opined that A.F.M.'s presentation of MFEI was within the upper age limit known for this epileptic disorder. Id.

He disagreed with Dr. Kinsbourne's opinion that the "vaccines received by A.F.M. resulted in the early onset of migrating focal epilepsy." Resp. Ex. F at 4. Even assuming that A.F.M. had a seizure on May 8, 2014, and that the seizure marked the beginning of her epilepsy, Dr. Holmes did not agree that she would have had a better outcome if the onset of her epilepsy had been delayed. Resp. Ex. G at 3. Citing studies about children with Dravet syndrome, Dr. Holmes opined that age of onset is not correlated to outcome. Id. Instead, he explained that disease severity is more likely associated with the severity of a child's genetic phenotype. Id.

Moreover, Dr. Holmes testified that none of A.F.M.'s treating physicians attributed her epilepsy to vaccination. Tr. 127. Instead, they believed there was a genetic or metabolic cause. Id. Genetic testing was done but it did not reveal the specific genetic condition. Id.

In conclusion, Dr. Holmes opined that there is no evidence that the vaccinations "precipitated the onset of [A.F.M.'s] epilepsy or had any effect [] on her eventual outcome." Resp. Ex. F at 4.

#### 3. Althen Prong Three

Dr. Holmes opined that there was not a medically appropriate temporal relationship between A.F.M.'s DTaP vaccination and her epilepsy. Tr. 128. He opined that from the time of A.F.M.'s initial event on May 8, 2014, it was 46 days before she had "what clearly was a seizure" and the development of epilepsy. Id. Dr. Holmes testified that Dr. Kinsbourne did not provide any mechanism that would explain how the initial event (seizure or ALTE) could lead to the development of epilepsy after 46 days. Id.

## IV. LEGAL STANDARDS

### A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the

vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, Petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the [R]espondent in determining whether the [P]etitioner has established a prima facie case." Flores v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 157, 162-63 (2014); see also Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

### B. Factual Issues

Petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding her claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records).

Medical records, specifically contemporaneous medical records, are presumed to be accurate and generally "warrant consideration as trustworthy evidence." Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). But see Kirby v. Sec'y of Health & Hum. Servs., 997 F.3d 1378, 1382 (Fed. Cir. 2021) (rejecting the presumption that "medical records are accurate and complete as to all the patient's physical conditions"); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 538 (2011) ("[T]he absence of a reference to a condition or circumstance is much less significant than a reference which negates the existence of the condition or circumstance." (quoting Murphy v. Sec'y of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991), aff'd per curiam, 968 F.2d 1226 (Fed. Cir. 1992))), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013). The weight afforded to contemporaneous records is due to the fact that they "contain information supplied to or by

health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." Id. To overcome the presumptive accuracy of medical records, a petitioner may present testimony which is "consistent, clear, cogent, and compelling." Sanchez v. Sec'y of Health & Hum. Servs., No. 11–685V, 2013 WL 1880825, at *3 (Fed. Cl. Spec. Mstr. Apr. 10, 2013) (citing Blutstein v. Sec'y of Health & Hum. Servs., No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)), mot. for rev. denied, 142 Fed. Cl. 247 (2019), vacated on other grounds & remanded, 809 F. App'x 843 (Fed Cir. 2020).

There are situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. Campbell v. Sec'y of Health & Hum. Servs., 69 Fed. Cl. 775, 779 (2006) ("[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking."); Lowrie v. Sec'y of Health & Hum. Servs., No. 03–1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." (quoting Murphy, 23 Cl. Ct. at 733). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley, 991 F.2d at 1575.

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining onset of a petitioner's symptoms. Valenzuela v. Sec'y of Health & Hum. Servs., No. 90–1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); see also Eng v. Sec'y of Health & Hum. Servs., No. 90–1754V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) "must be construed so as to give effect also to § 13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them").

### C. Table Claim

To receive compensation through the Program, Petitioner must prove either (1) that A.F.M. suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that A.F.M. suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Here, Petitioner alleges both a Table injury and a causation-in-fact injury. Pet. Mot. at 1. As acknowledged by Respondent, the alleged Table injury is based on the question of whether A.F.M. suffered an "encephalopathy." See Resp. Rept. at 16 (citing 42 C.F.R § 100.3(a)(II)(B)).

The Vaccine Injury Table provides that encephalopathy is a recognized injury for DTaP vaccinations if the first symptom or manifestation of onset occurs within 72 hours of vaccine administration. 42 C.F.R. § 100.3(a)(II)(B). A "vaccine recipient shall be considered to have suffered an encephalopathy if an injury meeting the description of acute encephalopathy occurs within the applicable time period and results in a chronic encephalopathy." Id. at § 100.3(c)(2).

Acute encephalopathy, for children less than 18 months of age, that presents without a seizure "is indicated by a significantly decreased level of consciousness that lasts at least 24 hours." Id. at § 100.3(c)(2)(i)(A)(1). Acute encephalopathy following a seizure "is demonstrated by a significantly decreased level of consciousness that lasts at least 24 hours and cannot be attributed to a postictal state—from a seizure or a medication." Id. at § 100.3(c)(2)(i)(A)(2). "Clinical features" that do not in themselves "demonstrate an acute encephalopathy or a significant change in either mental status or level of consciousness" include "sleepiness, irritability (fussiness), high-pitched and unusual screaming, poor feeding, persistent inconsolable crying, bulging fontanelle, or symptoms of dementia." Id. at § 100.3(c)(2)(i)(C). Moreover, "[s]eizures in themselves are not sufficient to constitute a diagnosis of encephalopathy and in the absence of other evidence of an acute encephalopathy, seizures shall not be viewed as the first symptom or manifestation of an acute encephalopathy." Id. at § 100.3(c)(2)(i)(D).

Exclusionary criteria for encephalopathy include, "[a]n underlying condition or systemic disease shown to be unrelated to the vaccine (such as malignancy, structural lesion, psychiatric illness, dementia, genetic disorder, prenatal or perinatal central nervous system (CNS) injury)." 42 C.F.R. § 100.3(c)(2)(ii)(A). The time period for first symptom or manifestation of onset of encephalopathy is less than or equal to 72 hours after DTaP vaccine administration. Id. § 100.3(a)(II)(B).

**D. Causation**

In the alternative, Petitioner alleges a causation-in-fact claim. To prevail on this claim, Petitioner must prove that a vaccine A.F.M. received caused her injury. To do so, Petitioner must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and A.F.M.'s injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for A.F.M.'s injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and A.F.M.'s injury ("Althen Prong Three"). § 13(a)(1); Althen, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. Petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen, 35 F.3d at 548-49. Petitioner cannot establish entitlement to compensation based solely on her assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether Petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in Petitioner's favor when the evidence weighs in her favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in Petitioner's favor).

Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. See Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying Petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). The Federal Circuit has made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan, 539 F.3d at 1351.

## V. ANALYSIS

### A. Initial Event May 8, 2014—Seizure or ALTE

As Federal Circuit precedent establishes, in certain cases it is appropriate to determine the nature of an injury before engaging in the Althen analysis. Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1346 (Fed. Cir. 2010). Since "each prong of the Althen test is decided relative to the injury[,]" determining facts relating to the claimed injury can be significant. Id. Here, the factual issue is whether A.F.M. had a seizure or an ALTE on May 8, 2014. Thus, before determining if Petitioner has met each prong of Althen, the undersigned addresses whether Petitioner has established, by a preponderance of the evidence, that A.F.M. suffered from a seizure on May 8, 2014, as alleged by Petitioner, or an ALTE, as suggested by Respondent.

The EMS records are the earliest-in-time documents about what happened the morning of May 8, 2014. They state that primary impression was "respiratory distress," and secondary impression was "seizure." Pet. Ex. 38 at 1. Chief complaints were "possible seizure like activity" and "apnea." Id. When EMS arrived at the home, A.F.M. was in her "grandmother's lap, unresponsive." Id. at 2. There was no seizure activity observed by EMS. Petitioner described finding A.F.M. earlier with her "arms extended out" and "eyes rolled back." Id. A.F.M. was not breathing. The record does not state that Petitioner or the grandmother reported any tremors, jerking, or convulsions. EMS personnel were Freddy Wright and Jeffery Beach; the certification level of these two personnel was not documented. See Pet. Ex. 38 at 3. Thus, their medical training and experience is not known.

On arrival to the ED, assessment was performed by Tiffany Koller, RN. Nurse Koller's initial note documents that Petitioner "state[d] child was sleep[ing] with her this [morning], awoke and noted [A.F.M.] was limp and staring off at ceiling, state[d] child was not responsive initially. EMS report[ed] child was not responding appropriately on arrival to the ED. Became more alert during transport[,] . . . on arrival in [ED] [A.F.M.] alert, playful." Pet. Ex. 8 at 53.

A.F.M. was assessed by Dr. Ervin whose history states that Petitioner found A.F.M. "staring off and [] unresponsive and limp[]." Pet. Ex. 8 at 67. Petitioner also reported that when she suctioned A.F.M., she obtained "a lot of material, that looked like saliva, and mucous

drainage out of her mouth and nose." Id. Petitioner denied that A.F.M. had any fever. Petitioner also reported a history of "spitting up/reflux." Id. at 68. The notes do not document that the family reported observing seizure activity or tremors, jerking, or convulsions. A.F.M. did not have any seizure activity in the ED. Dr. Ervin's impression was "[URI], episode of altered mental status, suspect possibly secondary to a reflux or choking episode, but she did not have any cyanosis. Possible [UTI]." Id. at 69. Dr. Ervin did not diagnose A.F.M. with a seizure.

An EEG was performed on May 13, 2014 and was normal. At her follow-up visit to her pediatrician on May 14, A.F.M. was found to be stable with no neurological abnormalities.

Dr. Kinsbourne testified that the physicians who cared for A.F.M. were "impressed by the fact that [Petitioner] told them that she had apnea, which means she stopped breathing, so they were thinking what causes apnea. And perhaps she choked on something, but she had an infection of [] the airways. They didn't know." Tr. 44. This statement by Dr. Kinsbourne is an acknowledgment that the physician did not assess A.F.M. with a seizure. Dr. Kinsbourne also agrees that A.F.M. was not diagnosed with a seizure at this time. See id.

Further, while Dr. Kinsbourne opines that A.F.M. had a seizure the morning of May 8, he offers inconsistent opinions about the type of seizure she had. He opines that A.F.M. had an absence seizure, NCSE, a prolonged absence seizure, and a hypomotor seizure. His inconsistency rendered his opinions less reliable, and he seemed much less knowledgeable especially as compared to Dr. Holmes.

Moreover, Dr. Kinsbourne stretches the facts when he opines that A.F.M.'s episode on May 8 was NCSE or a prolonged absence seizure, exceeding 30 minutes in duration. She did have a period of unresponsiveness that lasted approximately 16 to 20 minutes, but unresponsiveness is not the same as a seizure. Simply put, there is no persuasive evidence to support Dr. Kinsbourne's assertion that A.F.M. had a seizure that lasted 30 minutes or longer.

In contrast, Dr. Holmes opines that A.F.M. had an ALTE on May 8 because the information in the record did not allow one to conclude that A.F.M. had a seizure. Dr. Holmes appears to have embraced the conclusions of the treating physician, Dr. Ervin, who diagnosed A.F.M. with "[URI], episode of altered mental status, suspect possibly secondary to a reflux or choking episode, but she did not have any cyanosis. Possible [UTI]." Pet. Ex. 8 at 69.

The history given by the family to Dr. Terayanont, noting that June 22, 2014 was "the third time" that A.F.M. had the symptoms, suggests that the first event on May 8, 2014 may have been a seizure. However, Dr. Terayanont's description of "jerking movement of both upper extremities" is different than what was documented on May 8. Pet. Ex. 9 at 7. The contemporaneous records from May 8 do not describe jerking movement of both upper extremities. The EMS record states that the family reported the "[patient] found with arms extended out, eyes rolled back, not breathing." Pet. Ex. 38 at 2. Dr. Ervin documented the event as "altered mentation, staring spell, limp," quoting Petitioner as stating that A.F.M. was "barely breathing, limp, and gasping for air." Pet. Ex. 8 at 48.

Greater weight is typically given to contemporaneous records. See, e.g., Vergara v. Sec'y of Health & Hum. Servs., No. 08-882V, 2014 WL 2795491, at *4 (Fed. Cl. Spec. Mstr. May 15, 2014) ("Special Masters frequently accord more weight to contemporaneously-recorded medical symptoms than those recorded in later medical histories, affidavits, or trial testimony."). The weight afforded to contemporaneous records is due to the fact that they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." Cucuras, 993 F.2d at 1528; see also Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326.

Because the record by Dr. Terayanont on June 22 is different than the earlier-in-time records documented by three different health care providers (EMS, nurse, and physician) on the date of the May 8, 2014 event, the undersigned finds the earlier records are more reliable. Further, Dr. Holmes' opinion that A.F.M. had an ALTE is more consistent with the contemporaneous medical records and opinion of the treating physician.

The undersigned finds by preponderant evidence that on May 8, A.F.M. had an episode where she was found with her arms extended, eyes rolled back, limp and staring off at the ceiling, and not breathing or barely breathing. A.F.M. was suctioned and had saliva and mucous drainage from her mouth and nose. A.F.M. was diagnosed with an URI, episode of altered mental status, suspected to be possibly secondary to a reflux or choking episode, but she did not have any cyanosis. A.F.M. was not diagnosed with a seizure. Based on these factual findings, the preponderant evidence establishes that the event on May 8, 2014 was not a seizure but an ALTE. The undersigned specifically rejects Dr. Kinsbourne's opinion that A.F.M. suffered a prolonged seizure or status epilepticus.

**B. Table Claim**

Petitioner alleges that "[p]rior to the administration of her May 7, 2014[] vaccinations, the minor [A.F.M.] was in good health, except for minor cold symptoms and suffered no medical conditions." Petition at ¶ 3. "After receiving the vaccinations . . . [A.F.M.] suffered table[] injuries, including, but not limited to severe static epileptic encephalopathy and permanent brain damage." Id. at ¶ 4. Petitioner further alleges that A.F.M.'s Table injuries were caused by "one or more of her May 7, 2014 vaccinations." Id. at ¶ 16.

The question relevant to Petitioner's Table claim is whether A.F.M. sustained an injury consistent with acute encephalopathy within 72 hours of her DTaP vaccination. Pursuant to the Vaccine Injury Table, acute encephalopathy is defined as "a significantly decreased level of consciousness that lasts at least 24 hours." 42 C.F.R. § 100.3(c)(2)(i)(A)(1). A seizure does not, in and of itself, constitute evidence of a decreased level of consciousness. Moreover, "[t]he symptoms associated with an acute encephalopathy are neither subtle nor insidious." Blake v. Sec'y of Health & Hum. Servs., No. 03-31V, 2014 WL 2769979, at *6 (Fed. Cl. Spec. Mstr. May 21, 2014) (quoting Waddell v. Sec'y of Health & Hum. Servs., No. 10-316V, 2012 WL 4829291, at *6 (Fed. Cl. Spec. Mstr. Sept. 19, 2012)).

A.F.M.'s medical records establish that on May 7, 2014, the day of her DTaP vaccination, she was examined by a nurse practitioner, and noted to have a cough and runny

nose, but otherwise was normal and developmentally appropriate. See Pet. Ex. 7 at 15-19. The following morning, May 8, 2014, a call was placed for an ambulance at 5:34 a.m. Pet. Ex. 38 at 2. The ambulance arrived on the scene at 5:46 a.m. Id. Upon arrival, EMS found A.F.M. in her "grandmother's lap, unresponsive" with "respirations irregular and labored." Id. Lung sounds were clear, pulse was regular, and her skin was pale. Pupils were dilated and non-reactive. EMS did not document that A.F.M. was having seizure activity when they arrived. EMS records show that at 5:48 a.m., A.F.M. had a pulse of 140, respiratory rate of 20, and oxygen saturation of 88% on room air. Oxygen was administered and A.F.M.'s oxygen saturation improved to 92%. At 5:54 a.m., A.F.M. was noted to be "improved." Id. Assessment documented at 5:48 a.m. revealed no mental abnormalities, no abnormalities of the head, face, eyes, or airway, and no abnormalities of lung sounds. EMS departed the home at 5:59 a.m. and arrived at the ED at 6:22 a.m. Again, A.F.M.'s condition was noted to be improved. In their narrative notes for the event, EMS documented that the A.F.M.'s "condition gradually improved to normal response for age" and remained stable for the "duration of the trip." Id.

The ED records on May 8, 2014 at 6:30 a.m. document that A.F.M.'s condition on arrival was stable, and she was alert and playful. Her eyes were open; she was babbling and obeying commands. The ED physician (Dr. Ervin) was at the bedside at 6:40 a.m. to examine A.F.M. At 6:50 a.m., A.F.M. was again noted to be "awake, happy, [and] playing." Pet. Ex. 8 at 49. Neurological examination revealed that she was oriented and had no motor or sensory deficit. At 10:48 a.m., A.F.M.'s condition was "good stable." Id. at 59. Dr. Ervin's impression was "[URI], episode of altered mental status, suspect possibly secondary to a reflux or choking episode, but she did not have any cyanosis. Possible [UTI]." Id. at 69.

Nursing neurological system assessment performed on May 8, 2014 at 11:35 a.m. documented that A.F.M. was alert, that her behavior was appropriate, and that her assessment was within defined neurological parameters. A.F.M. was noted to be awake, cooperative, and smiling at 12:14 p.m. Progress notes at 1:13 p.m. document that A.F.M. was "awake and alert, baby appear[s] appropriate for age. Pleasant affect. No acute distress." Pet Ex. 8 at 81. During nursing rounds at 6:29 a.m., A.F.M. was again noted to be awake, cooperative, and smiling. Throughout the evening and overnight, A.F.M.'s assessments remained stable with no indication of abnormal neurological behavior. On May 9, 2014, at 5:16 a.m., A.F.M. was "awake" and "cooperative." Id. at 89.

A.F.M. was discharged on May 9, 2014 at 9:46 a.m., and her physical examination prior to discharge was normal. There is no indication that A.F.M. had any decreased or abnormal level of consciousness during her hospitalization. On May 13, 2014, A.F.M. had an EEG, which was normal. There is no indication that she had a decreased or abnormal level of consciousness at that time. A.F.M. was seen by her pediatrician, Dr. Crick, on May 15, 2014. Dr. Crick documented that A.F.M. had no problems following her hospital discharge; her physical examination was normal.

The medical records on May 8, 2014 show that A.F.M. experienced a period of unresponsiveness that began a few minutes prior to 5:34 a.m., when the family placed an emergency call. By 5:48 a.m., she had improved and was no longer unresponsive. Assessments

during A.F.M.'s hospitalization from May 8 through May 9 do not show any episodes of altered mental status, decreased level of consciousness, or neurological dysfunction.

Based on the medical records, Dr. Holmes testified that A.F.M. had a period of altered mental status for approximately 16 to 20 minutes. Tr. 156. Dr. Kinsbourne offers two different opinions as to the duration of the seizure and/or period of unresponsiveness on May 8. First, he opined that it lasted 41 minutes and then he opined it exceeded 30 minutes. Compare Pet. Ex. 41 at 3, with Pet. Ex. 43 at 1.

Specifically, Dr. Holmes opines that when A.F.M. was seen on May 8, 2014 after the event, she "respond[ed] normally although she had congestion which had begun a week prior to immunizations." Resp. Ex. A at 20. After her event on May 8, Dr. Holmes testified that A.F.M. did not have alterations in awareness, alertness, or behavior. She had no weakness, sleep disturbance, or fever. No neurological abnormalities were documented. She had a normal EEG and normal neurological examination on May 13. At A.F.M.'s follow-up visit on May 14, 2014, she was normal. Her MRI was also normal. Based on all these facts, Dr. Holmes opines that it was "inconceivable" that A.F.M. had inflammation of the brain. Tr. 126. He concludes there is no evidence that any injury occurred following A.F.M.'s vaccinations on May 7, 2014. Id.

The undersigned finds that Dr. Holmes' opinions are persuasive because they are consistent with the medical records which document numerous assessments performed by nurses and physicians from the period shortly after A.F.M.'s event on the morning of May 8, until her discharge on May 9. Thereafter, there is no evidence that A.F.M. had any neurological abnormalities after her discharge. She was seen on May 13 for her EEG and was noted to have a normal EEG with no evidence of epileptiform or focal abnormalities. Then on May 14, she was seen by her physician, and again, the records do not document any neurological abnormality. The evidence does not establish that A.F.M. had a "significantly decreased level of consciousness" for a 24-hour period during the first 72 hours following her vaccinations. 42 C.F.R. § 100.3(c)(2)(i)(A)(1).

Thus, Petitioner has not shown by preponderant evidence that A.F.M. suffered encephalopathy within 72 hours of her DTaP vaccination. Therefore, the undersigned finds that Petitioner has failed to prove a Table claim by preponderant evidence.

### C. Causation-in-Fact

Petitioner has also asserted a causation-in-fact claim, alleging that A.F.M.'s injury was caused by the DTaP vaccination that she received on May 7, 2014. Fundamental to this claim is Petitioner's assertion that the event on May 8, 2014 was the "onset seizure" that led to A.F.M.'s epilepsy. Because the undersigned finds that Petitioner failed to prove by preponderant evidence that the event on May 8 was a seizure, her causation theory also fails. If A.F.M. did not have an "onset seizure" on May 8, then there was no vaccine-related seizure that played a casual role in triggering her epilepsy, as posited by Dr. Kinsbourne.

For the sake of completeness, however, the undersigned analyzes Petitioner's cause-in-fact claim assuming that the event on May 8 was a seizure. The undersigned finds that even if

Petitioner had proven that A.F.M. had a seizure on May 8, she has failed to provide preponderant evidence of all three Althen prongs, as described below.

### 1. Althen Prong One

Under Althen prong one, Petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support his theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen, 618 F.3d at 1347 ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

Dr. Kinsbourne opines that the DTaP vaccination can cause, through an innate immune response, the release of proinflammatory cytokines which can trigger afebrile seizures[81] in an infant with a lower seizure threshold due to a genetic susceptibility, and that the triggered afebrile seizure can lead to epilepsy and epileptic encephalopathy. See Pet. Ex. 44 at 2.

Fundamental to Dr. Kinsbourne's theory is that afebrile seizures are caused by the DTaP vaccination through a cytokine driven process. The parties filed medical articles about afebrile seizures, but this information does not support Dr. Kinsbourne's opinions that the causal mechanism is a cytokine driven process specifically. Dr. Kinsbourne cited several articles that discuss seizures in the context of an afebrile infant, but they do not attribute afebrile seizures to a cytokine driven process by the DTaP vaccination. von Spiczak et al. noted that single afebrile seizures were reported in 44 (17.8%) of 247 cases but it is not clear what vaccines were administered prior to these afebrile seizures. See Pet. Ex. 39L at 2. Further, the authors do not conclude that afebrile seizures are caused by cytokines or cytokine driven inflammation. And the article does not offer any opinions about cytokines relative to vaccination.

In Verbeek et al., a study of vaccine-related seizures, the majority of children had febrile seizures, although three children developed epilepsy characterized by a lack of fever sensitivity. In two of the three, there was a history of familial epilepsy, "compatible with autosomal dominant inherited epilepsies" (genetic abnormalities). Pet. Ex. 37M at 9. The other child (case 23) with afebrile seizures had a negative family history. The authors concluded that "the large variability in electroclinical syndromes and corresponding cognitive outcomes in [the] study further support[ed] the hypothesis that predisposing factors within the child, and not the

[81] Both experts agree that A.F.M. was afebrile before the initial event on May 8, 2014. See Pet. Ex. 39 at 6; Resp. Ex. A at 21; Tr. 53, 126, 180.

vaccination, caused the observed neurological deterioration." Id. at 10. Verbeek et al. did not conclude that the DTaP vaccination causes cytokine-induced inflammation that leads to epilepsy.

In a variation on this theme, Dr. Kinsbourne also seems to suggest that the DTaP vaccination can lower a child's seizure threshold. He opines that if a "child's seizure threshold has already been lowered by a genetic abnormality, then even a usually harmless proinflammatory response can suffice to lower seizure threshold further" triggering a seizure. Pet. Ex. 44 at 2-3. However, he does not offer evidence that the DTaP vaccination, through cytokines, or any other proinflammatory or immune process, lowers a child's seizure threshold absent fever. Moreover, he does not provide evidence to show that an afebrile response to the DTaP vaccination ("harmless proinflammatory response") lowers the seizure threshold. In summary, there is evidence that the DTaP vaccination can cause fever, and that fever can trigger seizures, but this evidence does not extend to afebrile seizures or the facts here.

Another important tenet of Dr. Kinsbourne's causal theory is the presence of a genetic susceptibility which triggers a lowered seizure threshold. Both experts agree that there is an underlying genetic abnormality that is the cause of A.F.M.'s seizure disorder, although the specific abnormality has not been identified. Because the genetic abnormality is not known, however, it is not known whether it could cause a lower seizure threshold or render a child susceptible to an afebrile seizure. While there is evidence that children with some genetic disorders may have seizures with only mild elevations in temperature,[82] there is no evidence of such here. As such, there is no foundational evidence of a lowered seizure threshold.

Lack of information about a specific mechanism to prove that a theory is sound and reliable by preponderant evidence does not preclude Petitioner from prevailing. Given the state of current scientific knowledge, there is no way that a petitioner could satisfy such a requirement. And requiring proof of such would require scientific certainty, which is a bar too high. See Knudsen, 35 F.3d at 549 (explaining that "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program"). However, there must be more than speculation. Special masters consistently reject "conclusory expert statements that are not themselves backed up with reliable scientific support." Kreizenbeck v. Sec'y of Health & Hum. Servs., No. 08-209V, 2018 WL 3679843, at *31 (Fed. Cl. Spec. Mstr. June 22, 2018), mot. for rev. denied, decision aff'd, 141 Fed. Cl. 138, aff'd, 945 F.3d 1362 (Fed. Cir. 2020).

Another basic tenet of Dr. Kinsbourne's theory relates to cytokine-induced excitability. He cites Vezzani and Barum to support his opinion that proinflammatory cytokines "transform a normal brain to an epileptic one." Pet. Ex. 37N at 1. The authors discuss cytokine-induced hyperexcitability, particularly in the context of temporal lobe epilepsy and status epilepticus.

[82] Dr. Kinsbourne cited Dube et al. which "found that unlike control mice, IL-I beta deficient 'knock out' mice could not be stimulated by hyperthermia to cause febrile seizures." Pet. Ex. 39 at 4 (citing Pet. Ex. 39E (Celine Dube et al., Interleukin-1β Contributes to the Generation of Experimental Febrile Seizures, 57 Annals Neurology 152 (2005))). "It appear[ed] that the proinflammatory cytokines [were] the critical element rather than the rise in temperature per se and that IL-1 beta can generate seizures with little or no detectable temperature elevation." Id.

They conducted an animal study whereby "chemical or electrical means" were used to "stimulate[] a massive inflammatory response in the brain that consist[ed] of increased levels of cytokines, including IL-1β." Id. at 2. The study, however, did not replicate the facts here involving a possible afebrile seizure or a scenario where there is no evidence of a "massive inflammatory response."

Further, the authors explain that the "formation of a hyperexcitable circuit may depend on a "functional . . . abnormality in the case of epilepsies involving genetic causes." Pet. Ex. 37N at 1. This observation is important here, where both experts agree that there is a genetic cause of the relevant seizure disorder, although the specific genetic cause and its corresponding functional abnormality have not been identified. Lastly, the authors discuss the role of IL-1β in the context of fever and febrile seizures and again, there is no evidence here of fever or febrile seizure. Moreover, vaccinations are not discussed.

In sum, cytokines may be released during an inciting event which may promote a hyperexcitable state, they may contribute to seizure-evoked neuronal cell death, and they may play a role in febrile seizures. See Pet. Ex. 37N. But the facts of this case do not establish that there was a fever associated with the event on May 8, 2014.

Dr. Holmes strongly disagrees that a single afebrile seizure could cause epileptic encephalopathy through the cytokine driven process, described by Dr. Kinsbourne, where there is no evidence of inflammation in the form of fever, no abnormal EEG, no evidence of inflammation on the MRI, and no neurological abnormalities. Although Dr. Holmes does agree that after many seizures, "the brain can become more excitable," he disagrees that the article that he co-authored with Dr. Ben-Ari proposed that "changes in excitability lead to epilepsy." Tr. 134. Dr. Holmes and Ben-Ari explained that "the immature brain is more prone to seizures than the mature brain because of a developmental mismatch between the delicate balance of excitation and inhibition." Resp. Ex. A, Tab 26, at 5. They concluded that "prolonged or recurrent seizure activity, through activity-dependent mechanisms, can irreversibly alter the way the immature brain develops and forms synapses. This alteration in normal neuronal connectivity can result in long-term consequences in seizure susceptibility, learning and memory, and risk for subsequent seizure-induced injury." Id. at 5. The key words here are "prolonged" and "recurrent seizure activity." Again, the facts and circumstances here do not illustrate an onset event that was either prolonged or characterized by recurrent seizure activity.

The undersigned has previously found that in certain circumstances, post-vaccination febrile seizures may be associated with an increased risk of subsequent epilepsy, where experts agreed that vaccinations triggered the initial febrile seizure and there was evidence that the seizure was a focal (complex) seizure. See Ginn v. Sec'y of Health & Hum. Servs., No. 16-1466V, 2021 WL 1558342 (Fed. Cl. Spec. Mstr. Mar. 26, 2021); Fuller ex rel. B.F. v. Sec'y of Health & Hum. Servs., No. 15-1470V, 2019 WL 7576382 (Fed. Cl. Spec. Mstr. Dec. 17, 2019). Here, there is no evidence of a fever prior to the initial event on May 8, 2014, or that a fever triggered the initial event.

Moreover, the undersigned agrees with the reasoning set forth in a line of cases[83] where compensation has been denied by special masters in claims alleging that the DTaP vaccination caused afebrile seizures and epilepsy. See, e.g., McClellan ex rel. L.M. v. Sec'y of Health & Hum. Servs., No. 14-714V, 2019 WL 4072130, at *25-31 (Fed. Cl. Spec. Mstr. July 23, 2019) (finding that Petitioner's theory was deficient where he invoked a cytokine-based causation theory to support the position that vaccination triggered infant child's afebrile seizures); Walters v. Sec'y of Health & Hum. Servs., No. 15-1380V, 2023 WL 3750716, at *30 (Fed. Cl. Spec. Mstr. June 1, 2023), aff'd, 2023 WL 5274006 (Fed. Cl. July 31, 2023), appeal filed, Fed. Cir., Sept. 8, 2023; Nance v. Sec'y of Health & Hum. Servs., No. 06-0730V, 2010 WL 3291896, at *13 (Fed. Cl. Spec. Mstr. July 30, 2010) (denying entitlement in a DTaP/seizure disorder case because Petitioner's theory was speculative); Gram v. Sec'y of Health & Hum. Servs., No. 15-515V, 2022 WL 17687972 (Fed. Cl. Spec. Mstr. Nov. 16, 2022).[84]

Accordingly, the undersigned finds Petitioner has not offered a sound and reliable medical theory in support of her claim. Thus, Petitioner has not met the preponderant evidentiary standard with respect to Althen prong one.

### 2. Althen Prong Two

Under Althen prong two, Petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen,

[83] Older cases involving the whole cell pertussis vaccine, DTP, are distinguished based on the differences in the safety profiles between the whole cell and the acellular form of pertussis. See Pet. Ex. 37D; Pet. Ex. 37I; Pet. Ex. 39J (also cited as Resp. Ex. C, Tab 3); Resp. Ex. C, Tab 5 (Sheila Donnelly et al., Whole-Cell but Not Acellular Pertussis Vaccines Induce Convulsive Activity in Mice: Evidence of a Role for Toxin-Induced Interleukin-1b in a New Murine Model for Analysis of Neuronal Side Effects of Vaccination, 69 Infection & Immunology 4217 (2001)); Resp. Ex. C, Tab 6 (Klemons Stehr et al., A Comparative Efficacy Trial in Germany in Infants Who Received Either the Lederle/Takeda Acellular Pertussis Component DTP (DTaP) Vaccine, the Lederle Whole-Cell Component DTP Vaccine, or DT Vaccine, 101 Pediatrics 1 (1998)).

[84] But see Romero ex rel. Romero v. Sec'y of Health & Hum. Servs., No. 07-671V, 2010 WL 2766761 (Fed. Cl. Spec. Mstr. June 22, 2010). Romero is distinguishable based on its facts; the "onset seizure" was prolonged lasting between 20-30 minutes. Romero, 2010 WL 2766761, at *2-3. Two days later, the infant had another prolonged seizure lasting more than 30 minutes. Id. Thus, the child had two prolonged seizures within three days of vaccination.

418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

Since Petitioner failed to prove Althen prong one, it follows that she cannot prove Althen prong two. However, even if Petitioner had proven a sound and reliable causal mechanism, she failed to prove by preponderant evidence a logical sequence of cause and effect, showing A.F.M.'s DTaP vaccination caused her epileptic encephalopathy.

The first reason that Petitioner failed to prove prong two is that Petitioner has not shown evidence that A.F.M. had an increase in cytokine driven inflammation or excitability after vaccination. She did not have a fever, her EEG was normal, and her neurological examinations were normal after her initial episode on May 8, 2014. Dr. Kinsbourne concedes that there was no evidence that A.F.M. had inflammatory cytokines other than his contention that she had a seizure. Dr. Holmes opines that there was no logical sequence between vaccination and A.F.M.'s epilepsy because there was no evidence of an inflammatory response to the DTaP vaccination. A.F.M. had no fever, no weakness, no sleep disturbances, or alterations in awareness, alertness, or behavior. She had a normal EEG and MRI. The undersigned finds Dr. Holmes' opinions as to the lack of evidence of inflammation to be more persuasive, as they align with the facts set forth in the medical records.

Next, A.F.M. suffers from migrating focal epilepsy of infancy, or MFEI, a type of epilepsy known to be refractory to treatment and characterized by severe psychomotor delay. Dr. Kinsbourne concedes that most children with this disorder are severely impaired. And he also acknowledges that A.F.M. had a severe course consistent with most children. Based on the medical literature and opinions of Dr. Holmes, this type of epilepsy has not been associated with vaccinations. See Pet. Exs. 44A, 41B.

Further, there is no evidence to support Dr. Kinsbourne's opinion that if A.F.M. had not received her DTaP vaccination on May 7, her epilepsy would not have been as severe, or triggered as soon, or that it "deprived her of the chance to achieve further normal mental development pending any ultimate seizure onset." Pet. Ex. 42 at 4. The evidence on this issue includes the McIntosh et al. study of children with Dravet's syndrome (often caused by an SCN1A genetic mutation) that showed the mean age of seizure onset was earlier (7-8 weeks) in children with vaccine proximate seizures as compared to children whose onset seizures did not occur in relation to vaccinations. See Pet. Ex. 42G. However, there were no differences in other measures, including intellectual outcome. Thus, the McIntosh et al. study, even if applicable to a child who does not have Dravet's syndrome, does not provide evidence that A.F.M.'s condition would be different but for her DTaP vaccination. Instead, it supports Dr. Holmes' opinions that the DTaP vaccination did not change A.F.M.'s clinical course or outcome.

Lastly, both experts agree that A.F.M.'s condition was caused by an alternative factor, unrelated to vaccination. Here that alternative factor is a likely genetic abnormality. Dr. Kinsbourne opines that that A.F.M. had a "severe underlying" susceptibility, which was "inherited" and present from birth. Pet. Ex. 44 at 1. And he concedes that in the absence of her genetic predisposition, A.F.M. would have "most likely developed quite normally, vaccination or not." Id. Dr. Holmes agrees that the likely cause of A.F.M.'s epilepsy is genetic.

The undersigned acknowledges that Petitioner is not required to eliminate other potential causes in order to be entitled to compensation. See Walther v. Sec'y of Health & Hum. Servs., 485 F.3d 1146, 1149-52 (Fed. Cir. 2007) (finding Petitioner does not bear the burden of eliminating alternative independent potential causes). However, she finds it reasonable to consider "evidence of other possible sources of injury"—here, A.F.M.'s genetic abnormality—in determining "whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question." Stone, 676 F.3d at 1379.

In this case, "the presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination." Pafford, 451 F.3d at 1358-59; see also Walther, 485 F.3d at 1151 n.4 ("Where multiple causes act in concert to cause the injury, proof that a particular vaccine was a substantial cause may require the petitioner to establish that the other causes did not overwhelm the causative effect of the vaccine."). As such, the undersigned finds Petitioner failed to prove that the DTaP vaccine was the "but for" cause of A.F.M.'s condition.

For all of the reasons described above, the undersigned finds that Petitioner has failed to provide preponderant evidence of a logical sequence of cause and effect required under Althen prong two.

### 3. Althen Prong Three

Althen prong three requires Petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been equated to mean a "medically acceptable temporal relationship." Id. Petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro, 101 Fed. Cl. at 542

Dr. Kinsbourne opines that A.F.M.'s "onset seizure" occurred 16 hours after her DTaP vaccination. He specifically identifies the risk period of seizures with the DTaP vaccination as the first three days after vaccination. He further opines that A.F.M.'s epileptic encephalopathy was triggered by the DTaP vaccination given on May 7, 2018. Dr. Holmes disagrees and opines that there was not a medically appropriate temporal relationship between A.F.M.'s DTaP vaccination and her epilepsy. He opines that from the time of A.F.M.'s vaccination to the

development of epilepsy was 46 days.[85] Dr. Holmes testified that Dr. Kinsbourne did not provide any mechanism that would explain how the initial event (whether it was a seizure or ALTE) could lead to the development of epilepsy after 46 days.

The undersigned finds that A.F.M. did not exhibit signs or symptoms of epilepsy or encephalopathy within 72 hours of her DTaP vaccination, during the risk window identified by Dr. Kinsbourne. Therefore, the undersigned finds that there is not a medically appropriate temporal relationship between A.F.M.'s DTaP vaccination and her epilepsy and/or her epileptic encephalopathy.

Moreover, the undersigned finds Dr. Holmes' opinions on this issue more persuasive for two reasons. First, there is no evidence that A.F.M. had epilepsy or epileptic encephalopathy after her May 8 event. As described above, Dr. Holmes' opinions are consistent with the medical records which document numerous normal examinations and assessments performed by nurses and physicians from the period after A.F.M.'s event on the morning of May 8, until her discharge on May 9. See supra Section VI.B. There is no evidence that A.F.M. had any neurological abnormalities during this prior of time. A.F.M. had an EEG on May 13, and her EEG was normal with no evidence of epilepsy. On May 14, she was seen and evaluated by her pediatrician, and again, her examination was normal. A.F.M. did not have any seizure activity, neurological abnormality, and she was not assessed with epilepsy or encephalopathy. Therefore, there is no persuasive evidence of epilepsy or encephalopathy within 72 hours of the DTaP vaccination, the risk period identified by Dr. Kinsbourne.

A.F.M. was not diagnosed with epilepsy until after she experienced a seizure on June 22, 2014, and her EEG on June 23 was interpreted as abnormal. Thus, from the date of vaccination, May 7, until June 22, was a period of 46 days. Dr. Kinsbourne did not opine that onset was 46 days, nor did he explain how a period of 46 days would be appropriate given his cytokine driven theory.

Based on a review of all of the evidence, the undersigned finds that Petitioner has failed to prove by preponderant evidence that an onset of epilepsy and/or epileptic encephalopathy occurring 46 days after vaccination is an appropriate time frame to be temporally associated with the DTaP vaccination administered on May 7, 2014. Therefore, Petitioner has failed to provide preponderant evidence to satisfy Althen prong three.

## VI. CONCLUSION

A.F.M. has a severe illness, and her mother, Petitioner, has provided excellent and loving care to her daughter. The undersigned extends her sympathy to A.F.M. and Petitioner for all that they and their family have been through. The undersigned's Decision, however, cannot be decided based upon sympathy, but rather on the evidence and law.

[85] A.F.M. had a seizure on June 22, 2014, and an EEG performed June 23, 2024 was consistent with epileptic discharges. A.F.M. was diagnosed with "[s]eizure disorder" or epilepsy. Pet. Ex. 9 at 8.

For all of the reasons discussed above, the undersigned finds that Petitioner has not established by preponderant evidence that vaccination caused A.F.M.'s condition. Therefore, Petitioner is not entitled to compensation and her petition must be dismissed. In the absence of a timely filed motion for review pursuant to Vaccine Rule 23, the Clerk of Court **SHALL ENTER JUDGMENT** in accordance with this Decision.

**IT IS SO ORDERED.**

**s/Nora Beth Dorsey**
Nora Beth Dorsey
Special Master